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PROLONGED LABOR

CLINICAL EVALUATION

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The proper management of a long labor is one of the most difficult problems in obstetric practice. Long labor should be prevented if possible, but if prolonged labor does develop the physician should know how to provide the maximum safety for the mother and for the infant. He should be aware of the indications for, and the dangers of, operative intervention.

The purpose of this study is to evaluate clinically 158 cases of prolonged labor that occurred at Grady Memorial Hospital. The conditions found to be significant in these labors are discussed in their relationship to (1) the etiology, (2) the course of labor, (3) the indications for treatment, (4) the results for the infant, and (5) the type of labor to be expected if a later pregnancy occurs. For the cases reported here, the onset of labor is defined as the time at which the uterine contractions become painful and continue to produce dilatation and effacement of the cervix. The labor is considered as prolonged if the total elapsed time from the onset of labor until the delivery of the infant is 30 hours or longer and the infant weighs 1,500 gm. or more.

The 158 patients whose labors are evaluated in this paper were among a total of 19,159 women delivered under the supervision of the department of obstetrics and gynecology of Emory University at Grady Memorial Hospital between July 1, 1948, and Dec. 31, 1951. The incidence of prolonged labor was 0.8%. No maternal deaths occurred among the patients with prolonged labors during the years of this report. Stillbirths or neonatal deaths occurred in 33 infants of the 158 pregnancies, an infant mortality rate of 20.9%. The low incidence of prolonged labors and the high infant mortality rate reported here as compared with other studies [1] suggest that the onset of labor must have been timed rather strictly at Grady Memorial Hospital.

As a background for the interpretation of the results in this paper, the following information is given regarding the obstetric service at Grady Memorial Hospital. All of the patients are service cases and are delivered by the hospital house staff under the supervision of the members of the visiting staff of the department. The stillbirth rate for the service is 1.67%. The neonatal death rate is estimated at 2%; it cannot be determined accurately since it is necessary to discharge many patients very early in the puerperium because of a lack of bed space. The incidence of premature deliveries is 12%. The incidence of cesarean section during the years of this report was 0.72%.

ETIOLOGY AND INCIDENCE

Uterine inertia was the major cause for the prolonged labors in this study. Investigations have been made by other authors concerning the abnormal variations in uterine contractions and their significance in the etiology of prolonged labor.[2] The information in this report regarding the etiology of prolonged labor is limited to that which could be obtained from the clinical observation of the patients. Inertia was encountered in all except three, and in these the long labor was due to fetopelvic disproportion. Primary uterine inertia was encountered in 145 of the 158 patients. In 77% of all the cases, it occurred alone, without other complications such as disproportion. Because of the high incidence, it is evident that this paper is, in effect, a clinical evaluation of primary uterine inertia as a cause of prolonged labor. (The uterine inertia was secondary to oversedation or exhaustion in six patients, and in four it was secondary to fetopelvic disproportion.)

From the Department of Obstetrics and Gynecology, Emory University School of Medicine, and Grady Memorial Hospital.
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2. Hellman, L. M.; Harris, J., and Reynolds, S. R. M.: Characteristics of Gradients of Uterine Contractility During First Stage of True Labor, Bull. Johns Hopkins Hosp. **86**: 234-248, 1950. Jeffcoate, T. N. A.; Baker, K., and Martin, R. H.: Ineffective Uterine Action, Surg., Gynec. & Obst. **95**: 257-273, 1952. Reynolds, S. R. M.: Physiology of the Uterus, ed. 2, New York, Paul B. Hoeber, Inc., 1949, chap. 5.

The presence of a disproportion between the infant and the maternal pelvis was determined from a review of the clinical opinions during labor, the presentations and positions of the infants, roentgenologic pelvimetry studies, and the actual weights of the babies after delivery. As determined by these conditions, fetopelvic disproportion was observed in 31 patients, but in almost all cases the degree of the disproportion was borderline. The roentgenologic pelvimetry studies, in general, confirmed the clinical impressions regarding the pelvic capacity and the size of the fetus. Uterine inertia was present in all except three of the cases of disproportion. The poor uterine contractions made it difficult to appraise the extent to which the disproportion itself contributed to the prolonged labor. The inertia made it almost impossible to obtain a satisfactory "trial labor" in most of the patients with borderline disproportion. The complications in the labors of patients with disproportion caused the death of 12 babies, an infant mortality rate of 38.7%, as compared with a 16.5% infant loss among the patients without disproportion.

The incidence of the types of presentations and positions of the infant varied from those encountered in normal labors. For cephalic presentations the position that persisted throughout most of the labor was occiput anterior in only 33 patients (20.9%), occiput transverse in 51 patients (32.3%), occiput posterior in 57 patients (36.1%), and persistent occiput posterior in 4 patients (2.5%). The presentation of one infant was a transverse lie. Breech presentations occurred in 12 of the patients, an incidence of 7.6%. The breech deliveries were the only ones in which a definite relationship could be established between the presentation or position of the fetus and the prognosis for the infant. Of the 12 breech presentations, six babies did not survive.

The weight of the infants affected their survival. Half of the 14 babies that weighed 4,000 gm. or more did not live, even though some of them did not show any evidence of a fetopelvic disproportion. The infant mortality rate was approximately the same (33%) for the 6 premature infants and for the 22 infants with weights ranging from 3,650 to 4,000 gm. The mortality rate was the lowest (14.7%) for the 116 infants weighing from 2,500 to 3,650 gm.

The age of the mother influenced the prognosis for the infant. The 71 patients under 20 years of age lost seven babies. On the other hand, the 25 patients over 30 years of age lost 12 infants.

A study of the parity of the patients in this series showed that 85.4% were primiparas. The infant mortality rate was twice as great for multiparas as it was for the primiparas. The 135 primiparas lost 24 infants (17.8%), and the 23 multiparas lost 9 infants (39.1%). The labors of the multiparas were complicated by a high incidence of fetopelvic disproportion (11 cases), breech presentations (5 cases), and large infants (eight weighing 4,000 gm. or more). An interval of more than 15 years had elapsed since the last previous delivery for four of the multiparas. Incidentally, the 23 multiparas had delivered a total of 65 premature or term infants before the prolonged labor of this report. Ten of the 65 infants were premature, and 7 of these had died. Seven of the 55 term infants did not live. Although complete records of all of the 65 previous deliveries are not available, no case of fetopelvic disproportion was found. A prolonged labor occurred with an earlier pregnancy in five of the multiparas, but the infants of those labors lived.

Rupture of the amniotic membrane before the onset of labor occurred in 18 of the 158 prolonged labors, and in 17 of these the rupture was spontaneous. The incidence of the premature rupture of the membranes was about normal, but the infant mortality was unusually high since nine of the babies were lost. Although the artificial rupture of the membranes was used to induce labor in approximately 150 women during the years of this study, a prolonged labor occurred in only one of the patients. (At Grady Memorial Hospital labors are rarely induced by the artificial rupture of the membranes except for a toxemia of pregnancy.)

ARREST OF PROGRESS IN LABOR

Progress during the course of labor was determined by the descent of the presenting part of the infant into the pelvis or by the dilatation or effacement of the cervix. Progress was considered to be arrested if, during a period of several hours, no significant change occurred in the descent, dilatation, or effacement. The slowing of progress in labor as a result of therapeutic sedation was not considered as an arrest. In the 158 patients in this group, progress was arrested in 153 of the labors. The arrest occurred before the end of 24 hours of labor in 118 of the patients. Only 16 women continued in labor over 30 hours before progress stopped. The arrest was primarily a problem of the first stage of labor. The labor of 100 patients became arrested while the cervix was dilated 4 cm. or less. At the time of the arrest, the cervix was dilated more than 6 cm. in only 20 cases.

Progress usually became arrested with a cervical dilatation of 4 cm. or less and after approximately 18 to 24 hours of labor. The attending physician should seriously consider the use of sedation or stimulation if these conditions begin to develop in the course of labor. The proper use of sedation and stimulation might maintain normal progress in labor and prevent many of the later complications. From the information in this study, however, it was impossible to predict the final length of the labor or the result for the infant from the variations in the time and in the cervical dilatation when the progress stopped.

The prognosis for the infant at the time of the arrest of progress could be predicted from the station of the presenting part of the infant and from the status of the amniotic membrane, whether intact or ruptured. The infant mortality rate was 15.4% if the presenting part of the infant had become engaged by the time progress became arrested, but it was approximately twice as great (28.8%) if engagement had not occurred. It can be seen from table 1 that the condition of the amniotic sac at the time of the arrest was considerably more important than the station of the presenting part. If the membranes had already ruptured at the time of the arrest, the infant mortality rate was 38.3%, or four times as great as when the membranes were intact at that time. The prognosis for the infant at the time of the arrest was much better if the membranes were intact, even with the presenting part unengaged, than it was if the membranes were rup-

tured even though the presenting part had already become engaged. The combination of the two conditions gave a better indication of the danger for the infant. The prognosis was poorest if the arrest took place after the membranes had ruptured but the presenting part was still unengaged. Over half of the infants (54.2%) were lost. The infant mortality rate in these patients was seven times as great as it was among those in whom the membranes were still intact and the presenting part of the infant was engaged at the time of the arrest.

TREATMENT TO IMPROVE PROGRESS IN LABOR

The three methods usually suggested to improve the rate of progress in labor are: rest or sedation, artificial rupture of the amniotic membrane, and pituitary extract. It is not the purpose of this paper to outline a specific plan of treatment for patients with prolonged labor. The treatment given to the patients in this study is reviewed to the extent that it appeared to affect the duration and the result of their labors.

Morphine combined with barbiturates was used for the therapeutic sedation of the patients of this report, but it was not possible to demonstrate that the sedation consistently affected the course of labor either favorably or unfavorably. After therapeutic sedation, an occasional patient had a definite improvement in the rate of progress and delivered quickly. Generally, however, progress seemed to be improved very little after the use of sedation. Although no definite benefit could be attributed to the therapeutic sedation, we believe that it proved valuable in maintaining the general condition of the patients and thereby preventing exhaustion. Sedation for the purpose of the relief of pain in labor (for analgesia and amnesia) interferred with the normal progress of labor in four cases by producing a secondary uterine inertia.

The most effective therapy found in this study for improving the progress of labor after it had become arrested was the artificial rupture of the amniotic membrane. In 90 patients, the progress was arrested while the membranes were still intact, and eight babies were lost. The effectiveness of the artificial rupture of the membranes can be seen in table 2. If the membranes were not ruptured artificially, the infant mortality rate was 13%, and it was approximately the same whether or not engagement had occurred before the arrest of progress. If the membranes were ruptured artificially after the arrest had occurred, the infant mortality rate was 2.8%. No prolapsed umbilical cords occurred from the rupture of the membranes, whether the rupture was spontaneous or artificial.

The prognosis for the patient's labor after an arrest could be predicted by the response to treatment combining the rupture of the membranes with the use of pituitary extract (unless a contraindication for pituitary extract was present). If the progress in labor was satisfactory after these means of treatment were instituted, a successful vaginal delivery could be predicted. If the progress was not satisfactory, the likelihood of a successful vaginal delivery was slight. In a prolonged labor it is often quite difficult to determine whether the amount of progress within a given period of time should be considered as a satisfactory response. The decision is made more difficult by the uterine inertia that is usually present. Treatment consisting of the use of pituitary extract (unless contraindicated) after the rupture of the membranes should be continued only as long as a successful vaginal delivery can be expected. A vaginal delivery should be considered successful if the cervix dilates completely and if a normal child is delivered without injury to the mother. It should be considered unsuccessful if the patient is delivered by cesarean section, vaginally before complete dilatation of the cervix, or vaginally of an infant that does not survive.

From table 3 it can be seen that a successful vaginal delivery occurred in 114 patients. If the patients had not delivered within eight hours after the rupture of the membranes and the use of pituitary extract (unless contraindicated), a successful vaginal delivery occurred in only half of the 59 cases. Under these circumstances, serious consideration should be given to cesarean section at the end of eight hours of treatment unless vaginal delivery is imminent. If cesarean section had been employed for all of the cases of this report in which the delivery was

TABLE 1.—*Prognosis for the Infant at the Time of Arrest of Progress in Labor**

Station of Presenting Part at Time of Arrest	Condition of Amniotic Membrane at Time of Arrest: Ruptured — No. of Cases	Ruptured — Infants Died	Ruptured — % Infants Died	Intact — No. of Cases	Intact — Infants Died	Intact — % Infants Died	Totals — No. of Cases	Totals — Infants Died	Totals — % Infants Died
Unengaged	24	13	54.2	35	4	11.4	59	17	28.8
Engaged	36	10	27.8	55	4	7.3	91	14	15.4
Total	60	23	38.3	90	8	8.9	150	31	20.7

* Of the 158 cases of this report, arrest did not occur in the labors of 5 patients, and information concerning 3 others could not be secured; 2 infants were lost in the 8 cases not included.

TABLE 2.—*Effect of Artificial Rupture of Amniotic Membrane After the Arrest of Progress in Labor*

Station of Presenting Part	Membranes Not Ruptured Artificially: No. of Cases	Not Ruptured Artificially: Infants Died	Not Ruptured Artificially: % Infants Died	Membranes Ruptured Artificially: No. of Cases	Ruptured Artificially: Infants Died	Ruptured Artificially: % Infants Died	Totals: No. of Cases	Totals: Infants Died	Totals: % Infants Died
Unengaged	22	3	13.6	13	1	7.7	35	4	11.4
Engaged	32	4	12.5	23	0	0	55	4	7.3
Total	54	7	13.0	36	1	2.8	90	8	8.9

not imminent within eight hours after the treatment was begun, many disastrous operative procedures would have been avoided. The incidence of cesarean section for the 158 prolonged labors would have been 35%. If all of the infants from the additional cesarean sections had survived, the infant mortality rate for the study would have been 8%. Of course, as indicated by 14 cases in this report, it may become evident before the end of the eight hours of treatment that a successful vaginal delivery will not occur. In such patients, if cesarean section in indicated, it should not be delayed until the end of eight hours of treatment.

TABLE 3.—*Interval Between Treatment of Arrest in Labor by Pituitary Extract and/or Rupture of the Membranes and Delivery*

	Delivered Within 8 Hr. After Treatment Begun	Delivered Over 8 Hr. After Treatment Begun	Total
Successful vaginal delivery	85	29	114
Unsuccessful vaginal delivery	14	30	44
Total	99	59	158

Operative deliveries, as shown in table 4, were associated with a higher infant mortality rate than spontaneous deliveries. It is true, however, that 8 of the 22 infants that did not survive after operative delivery died in labor before the operation was begun. If these eight infants are combined with the infants delivered spontaneously, it is found that the 109 patients lost 19 infants (17.4%) without operative interference. An operative delivery was begun in 49 patients while the infant was still living, and 14 babies (28.6%) did not survive.

The evaluation of the operative procedures listed in table 4 reveals that the incidence of cesarean section was 7.6% for the 158 prolonged labors. Fetopelvic disproportion was a contributing factor in the indications for cesarean section in 10 of 12 patients. Although 121 women in this study had a prolonged labor associated with primary uterine inertia, without evidence of fetopelvic disproportion, only 2 of them were delivered by cesarean section. These two cesarean sections were not performed until after more than 80 hours of labor; both infants died. (The teaching of this department and of this hospital is that primary uterine inertia can be an indication for cesarean section. The information in this report demonstrates that such a policy is not carried out in practice.) The failure to perform cesarean sections for primary uterine inertia among the cases of prolonged labor in this report provides the opportunity of studying the results to be expected if all cases of primary uterine inertia are delivered vaginally.

TABLE 4.—*Method of Delivery of Infants*

	Spontaneous	Assisted Breech	Breech Extraction	Low Forceps	Midforceps, Anterior Position	Midforceps Rotation	Duhrssen's Incisions	Craniotomy	Cesarean Section	Total
Survived	90	5	1	7	5	6	2	0	9	125
Neonatal death	5	0	1	1*	0	3*	3	0	1	14
Stillborn	6†	2*	1	0	0	3	1	4‡	2	19
Total	101	7	3	8	5	12	6	4	12	158

* Three infant deaths occurred after gross errors in operative technique at deliveries.
† Tight loop of umbilical cord about the neck of two infants.
‡ One infant was hydrocephalic, a frank breech presentation. (One of the 12 breech presentations was delivered by cesarean section.)

RESULTS FOR THE INFANT

The methods used for delivering the infants of this report are summarized in table 4. The length of the labor affected the results for the infant. The infant mortality rate for the 115 patients whose labor lasted less than 48 hours was 13.9% (16 deaths). For the 19 women whose labor lasted from 48 to 60 hours, the infant mortality rate was 21.1% (4 deaths), and for the 24 women whose labor lasted 60 hours or longer the infant mortality was 54.2% (13 deaths).

The underlying causes of death for the infants in this study were predominantly intrapartum fever and operative procedures for delivery. The 43 cases of labors lasting over 48 hours included 21 patients whose labors were afebrile. These 21 women lost five infants, but three of the five were delivered by difficult operative procedures. Labors lasting over 48 hours, without fever and without operative deliveries, ended with the death of only two infants, and both of these were premature babies.

It is logical to expect intrapartum fever to increase the danger to the infant because of the increased oxygen requirements from the temperature elevation.[3] If the fever in labor is of long duration, the requirement of more oxygen for the fetus could easily become critical and could cause a greater number of infant disasters. Fever of 1 degree (F) or more developed during the labors of 52 patients. The fever began during the first 12 hours of labor in 14 of the women, and seven of the babies were lost. The 36 women with fever less than 36 hours before delivery lost six infants. By contrast, the 16 patients who had had fever over 36 hours before delivery lost 13 babies (81.2%).

The significance of intrapartum fever and of operative deliveries as causes of infant mortality becomes more impressive if they are considered together. Fever during labor was present before the death of the infant in 19 cases. Fourteen infants died when operative deliveries were started while the baby was still alive. Only five infants died that had not been delivered after febrile labors or by operative procedures. One of these five labors was in a mother with eclampsia, one labor ended in the rupture of the uterus, and one of the five infants had a tight loop of umbilical cord around its neck.

COMPLICATIONS IN LABOR

Unusual complications developed in the labor of 14 patients. Tetany of the uterus was observed during the labor of 10 women, and seven of the infants died. The

3. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 5, Baltimore, Williams and Williams Company, 1950, p. 621.

umbilical cord prolapsed while delivery was being attempted in two patients, and both infants were lost. Rupture of the uterus occurred in one case. It took place almost immediately after an intravenous clysis containing pituitary extract was begun to stimulate the labor of a multipara who was considered to have an adequate pelvis. A pathological retraction ring (Bandl's ring) developed in the labor of a patient with a hydrocephalic infant. The infant was a breech presentation, and the hydrocephalus was not recognized until the delivery began. The roentgenologic studies during labor had not demonstrated any deformity of the fetal head.

POSTPARTUM COURSE

Postpartum infections developed in 23 patients (14.6%). Endometritis was responsible for infection in 16 patients, parametritis in 2, pyelonephritis in 4, and bronchopneumonia in 1. Almost without exception, the morbidity in these patients was of short duration. Postpartum hemorrhage and shock were not a problem.

LATER PREGNANCIES

The subsequent pregnancies of the patients in this report were reviewed. By April 1, 1953, 77 of the 158 women had delivered a total of 101 premature or term infants after their experience of prolonged labor. The later pregnancies were strikingly normal in their duration and in the results for the infants. Only 16 of the 101 later labors lasted over 12 hours, and only 2 of these lasted over 24 hours. A prolonged labor occurred in only one later pregnancy. This labor lasted 31 hours, and it was terminated at that time by cesarean section. In the later pregnancies, three premature and two term infants died. Two of the five infants died before the onset of labor, and two premature infants, delivered after less than 12 hours of labor, died in the first day of life. One baby died after hemorrhage and shock developed during the labor of a patient with a placenta previa.

All except 12 of the later pregnancies were delivered spontaneously. Six women who had been delivered by a cesarean section at the prolonged labor of this report had eight later pregnancies again delivered by cesarean section. Two patients were delivered for the first time by cesarean section in a later pregnancy. The infant that died in the labor complicated by the placenta previa was delivered as an assisted breech. One 1,325 gm. infant, which died before the onset of labor, was delivered from a transverse lie by a version and extraction.

The later pregnancies of the women who had had primary uterine inertia in their prolonged labor were delivered after short labors, with the uterine contractions of normal character. Of 31 patients with fetopelvic disproportion complicating the prolonged labor, 13 had 17 later deliveries. Ten of the 17 later pregnancies were delivered by cesarean section.

SUMMARY

The 158 prolonged labors occurring among 19,159 deliveries are evaluated clinically. All of the mothers lived, but 33 of the infants died. Primary uterine inertia was present in the labor of 145 patients. It was the only etiological factor recognized clinically in 121 of the cases. Fetopelvic disproportion was found in 31 women, and 12 of the babies were lost (38.7%). The babies were delivered as breech presentations in 12 cases, and half of the infants died. Of the infants weighing 4,000 gm. or more, 50% did not survive. The age of the patient and her parity significantly affected the labor and its results. Patients over 30 years of age lost 50% of their babies. The patients were primiparas in 85% of the prolonged labors. Fetopelvic disproportion and/or presentations of the infant other than cephalic occurred in 65% of the multiparas.

Progress became arrested in 75% of the cases before labor had lasted 24 hours. The cervix was dilated not more than 4 cm. in 100 patients at the time that the arrest of progress occurred. If progress became arrested, with the membranes ruptured and the presenting part still unengaged, over 50% of the infants did not survive. The most effective treatment after the arrest of progress in patients with the amniotic membrane still intact was artificial rupture of the membranes. If the patients did not deliver within eight hours after the rupture of the membranes and the use of pituitary extract (unless contraindicated), the results obtained by vaginal deliveries were found to be unsuccessful in half of the cases. The 43 patients in labor over 48 hours lost 40% of their babies. The underlying causes of death for the infants were predominantly intrapartum fever or operative delivery. The patients who had had fever for more than 36 hours before delivery lost 81.2% of the infants. Elevated temperatures during labor or operative procedures at delivery occurred in all except two of the cases in which the infant died after 48 hours of labor.

The later pregnancies of the women whose prolonged labor had been caused by uterine inertia alone were delivered spontaneously, after short labors, with excellent results for the infant. In the patients with prolonged labor complicated by fetopelvic disproportion, over 50% of later infants were delivered by cesarean section.

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Tuberculosis.—Although we have thus artificially removed tuberculosis from our consciousness by removing its victim from our daily experience, the never-to-be-forgotten fact is that there are today some 35,000 to 40,000 persons with active tuberculosis in New York City alone, 400,000 in the United States, not to speak of the 50,000,000 tuberculous persons in the rest of the world. More than half of the adult population of our city reacts positively to tuberculin, a fact which proves that most of us are infected by contact with tuberculous persons in the course of our normal lives, and become, from then on, carriers of living, virulent bacilli. It is becoming evident that the morbidity rate is not falling as fast as the mortality rate. In New York City, for example, there were 17,645 known cases of pulmonary tuberculosis in 1931; the number was still 17,499 in 1952, 20 years later. And these figures do not tell the whole story, for it is well known that a large percentage of tuberculous patients (probably close to 50%) are never entered in official records and continue to forge unsuspected the chain of infection among their fellow men. In other words, we have been more successful in retarding death from tuberculosis than in protecting against infection or in curing the disease.—Rene J. Dubos, Biologic and Epidemiologic Aspects of Tuberculosis, *The American Review of Tuberculosis*, July, 1953.

CLINICAL OBSERVATIONS AND INTERPRETATIONS OF ABNORMAL AIR SPACES IN THE LUNGS

A NEW CONCEPT OF THEIR ORIGIN

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Abnormal air spaces in the lung parenchyma, such as cysts, bullae, and pneumatoceles, have been the subject of an increasing amount of discussion during the past 25 years. Large-scale roentgenographic surveys have revealed many such cases in which the lesions were clinically latent. Long-range observations have revealed their variable clinical evolution, and increasing numbers of surgical explorations have yielded data on their morphological features. All of this has thrown much new light on these remarkable pulmonary changes.

In view of all the accrued information there is now renewed discussion of cystic, bronchiectatic, and bullous lung changes. In recent literature there is increasing cognizance of the fact that these changes are related to each other and, in some manner, to emphysema, the essential basis of which is air space abnormality. Brief reading of current writings should convince us that there is now an urgent need for a better understanding of the pulmonary conditions associated with abnormal air space formation, since their incidence appears to be increasing and since we are beginning to make new approaches in treatment.

In a recent publication we have outlined a new concept of the common origin of cystic, bronchiectatic and emphysematous lung changes.[1] We will here discuss clinical observations and present the broader aspects of our concept by which all these phenomena can be reduced to the common denominator of air space disorder as a manifestation of abnormal lung function resulting either from developmental or from pathological changes in the lungs.

Some of the more important data regarding abnormal air spaces in the lungs gleaned from recent literature and borne out by our own observations are significant: 1. They are frequent clinical findings and their incidence appears to be increasing. 2. They are often present in a clinically silent state in otherwise healthy persons, revealed mostly as accidental roentgenographic findings. 3. Often they reveal themselves first by spontaneous pneumothorax, by sudden hemoptysis, by intercurrent infection, or by so-called pseudoasthma. 4. They are found at all ages and increase in frequency from childhood to advancing age. 5. In infants and children their incidence is already far beyond that conceivable for congenital anomalies. 6. They are often considered congenital, although clinical observation most frequently indicates acquired origin. This is so because there are often morphological features that to many pathologists suggest developmental rather than pathological origin. Against this origin, however, is the fact that such changes, are exceedingly rare in the newborn and stillborn.

The various lung changes under discussion here are so often found combined that great confusion in nomenclature has resulted in such descriptive terms as cysts, bullae, pneumatoceles, cystic bronchiectasis, cystic emphysema, bullous emphysema, pneumocysts, vanishing lungs, and honeycomb lungs. This indicates, however, their close relationship to one another and to emphysema.

Development of air space disorders has been observed at all ages in patients whose lungs previously appeared normal. In infants and children particularly it is not uncommon to see such lung changes appear and disappear, enlarge in size, or alter in number over prolonged periods of observation. Dilatations of bronchi, for example, bullae, and their combinations may appear and then disappear in infants a few days or weeks old, or they may be followed by the formation of permanent cysts, pneumatoceles, or cystic bronchiectases. In some cases cystic or bullous structures increase in size merely by hyperinflation, due to mechanical obstruction of abnormal air spaces, with compression and displacement of the surrounding lung. In other instances, these structures seem to have increased by atrophy of lung structures, resulting in truly "vanished" lungs. In hyperinflated air spaces reversibility is frequently observed. Complete reversibility has been accepted as the criterion of pneumatoceles, but considerable extent of reversibility is common also in other air space disorders with fluctuations in the degree of hyperinflation and in the degree of patency of bronchial obstruction.

Operation of check valve obstruction has been demonstrated for cysts and bullae as well as for pneumatoceles. This has led to such confusion that distinction between them in practice has become virtually impossible, although it is often insisted on in theory. It becomes clear that this theory is no longer feasible, from the fact that even morphological differentiation is nearly impossible.[2]

In bronchiectatic conditions, there may be cystic distention of structures in some areas, while in others saccular and cylindric changes prevail. Also, at times cystic structures have been seen to shrink subsequently into sacculated and cylindric bronchiectases. It has been increasingly shown that cystic and bronchiectatic changes in the lungs, described as honeycomb lungs, may be associated with and perhaps produced by metabolic disorders. These include xanthomatosis, biliary cirrhosis, tuberous sclerosis, diabetes insipidus, pancreatic and pituitary insufficiency, lipoid granulomatosis, scleroderma, and reticuloendotheliosis. Recent experience has also shown that in diffuse extensive granulomatosis and fibrosis of the lungs, bullous changes resembling cysts

Read before the Section on Diseases of the Chest at the 102nd Annual Meeting of the American Medical Association, New York, June 2, 1953.

1. Mayer, E., and Rappaport, I.: Developmental Origin of Cystic, Bronchiectatic and Emphysematous Changes in Lungs: New Concept, Dis. Chest **21**: 146 (Feb.) 1952.

2. Caffey, J.: On the Natural Regression of Pulmonary Cysts During Early Infancy, Pediatrics **11**: 48 (Jan.) 1953. Conway, D. J.: The Origin of Lung Cysts in Childhood, Arch. Dis. Childhood **26**: 504 (Dec.) 1951.

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are produced almost regularly if the process is severe enough. These include berylliosis, sarcoidosis, and atypical granulomatosis and fibrosis of the lungs. Furthermore, massive emphysema often develops acutely with abrupt production of bullae and cyst-like pulmonary changes in infants and young children afflicted with diffuse acute bronchopneumonias, especially of staphylococcic origin.

From clinical observations, borne out by recent literature, it is our impression that a shift from acute suppurative bronchiectatic to more chronic cystic and bullous changes is now taking place. With the advent of the antibiotic era a marked decrease has occurred in the incidence of bronchopulmonary suppurative processes associated with bronchiectatic changes, while that of cystic and bullous changes has increased. Suppurative bronchopulmonary processes treated with antibiotics are now frequently brought under control, leaving cystic residues indistinguishable from identical changes in cases without evidence or history of preceding inflammatory process. Also the clinicopathological picture of cystic residues of inflammatory processes and that of cysts complicated by infection are today more difficult to separate from one another.

CURRENT CONCEPTS AND PROBLEMS

The long list of confusing classifications of pulmonary air space abnormalities clearly shows that all efforts to bring order into their clinical and pathological interpretation have so far failed. The trend is to separate them into two groups: the developmental and the pathological. In the first group are classified localized abnormal air spaces characterized by morphological features that are interpreted by many pathologists as indicative of developmental origin; in the second group are classified localized or diffuse abnormalities the clinical appearance of which is much like that of emphysema. These are therefore identified with the latter and are looked on as manifestations or forms of it. The implications arising from these classifications have brought forth added problems.

Problem of Acquired Origin of Developmental Abnormalities.—Abnormal air spaces showing morphological features of a developmental nature have been generally accepted as indicative of congenital origin. At the same time, however, clinical observations have established that all but an insignificant few are of acquired origin. With this conflict there arose the problem of reconciling the features of developmental nature with those of acquired origin. In a recent publication [1] we discussed a concept that seemed a reasonable answer. We postulated that abnormal air spaces may develop on the basis of developmental defects that have arisen during the postnatal period of growth of the lungs, when metabolic disturbances have interfered with their normal postnatal development. In clinically manifest severe insufficiencies of pancreatic, hepatic, and pituitary origin, the metabolic disturbances are commonly associated with cystic and bronchiectatic lung changes. It is logical to assume that metabolic disturbances of lesser degrees interfering to a lesser extent with postnatal lung development may yet leave developmental defects in the lungs in latent form.

Substantial support in favor of this was found by Medlar [4] in recent pathological studies. He interprets his findings as indicating that developmental defects account for the origin of all bronchiectatic and some cystic changes in the lungs. Clinical observations have established the fact that bronchiectatic, cystic, and emphysematous lung changes are practically inseparable. We believe therefore that latent developmental defects may evolve later into abnormal air spaces, manifesting themselves in cystic and bullous changes. When such changes are present in localized form, it is a reasonable assumption that they could have originated in localized developmental defects. In lung areas so affected normal lung function has obviously failed to develop from the start. How this may be linked up with the broad concept of air space formation as the normal visceral lung function that begins at birth will be discussed later. At this point it should be noted that there is suggestive evidence that developmental defects imply a disturbance in the autonomic regulation of the visceral lung function.[5] In this sense then, the abnormal air spaces to which they subsequently give rise may be interpreted as manifestations of disturbed visceral lung function restricted to localized areas. Since this function does not begin until birth, obviously abnormal air spaces can be acquired only after that.

Problem of the Primary Factor in Localized Air Space Abnormalities.—The prevailing opinion is that localized abnormal air spaces are produced by an obstructive check valve mechanism and that their clinical behavior bears this out. We believe, however, that these observations merely indicate that check valve obstruction plays an important role in the clinical evolution of localized cystic and bullous changes. Certainly when lung changes show developmental features, obstructive hyperinflation is only a secondary factor accounting for the progressive increase of an already preexisting abnormal air space.

Clinical observations indicate that no distinction is possible between lung changes with or without developmental changes. In abnormal air spaces produced by pathological processes, it is a reasonable assumption that such changes at the site play the primary role. It may also be assumed that in all abnormal air spaces where check valve obstruction hyperinflates, this is preceded by such an abnormality. We believe that check valve obstruction brings about excessive hyperinflation only in the presence of abnormal air spaces at the site affected, and that check valve obstruction is not the only factor in the mechanical overdistention of abnormal air spaces. The operation of still another mechanism, is to be discussed later.

The pathological findings of Medlar not only have confirmed our concept but have also shown that developmental defects are so localized and restricted in extent that they remain clinically latent, invisible, and undemonstrable by clinical examination. When mechanical factors supervene, they cause overdistention, so that the developmental defects become clinically manifest. Localized abnormal air spaces should therefore be looked on as overdistended defects of developmental or pathological origin. The real problem here is the primary factor that makes this lung defect subject to mechanical over-

4. Medlar, E.: Personal communication to the authors.
5. Ayers, W. B.; Stowens, D., and Ochsner, A.: Fibrocystic Disease of Pancreas, J. A. M. A. **142**: 7 (Jan. 7) 1950.

distention. In the interpretation of air space abnormalities, this has been given little consideration.

Problem of Emphysema as the Key to Abnormal Air Spaces.—Pulmonary emphysema has become the key to the origin and nature of abnormal air spaces. Its prevailing concept is that of mechanical overdistention of air spaces, and since abnormal air spaces are mechanically overdistended, they are considered to be manifestations of emphysema. In localized forms, check valve obstruction of the bronchi is presumed to play the key role. In diffuse forms, generalized bronchoconstriction is considered as the primary factor. Yet it has long been recognized that localized, as well as diffuse, forms of emphysema are often present without bronchial obstruction. Giant bullae in both lungs are often observed in persons showing no signs of bronchial obstruction clinically, and this cannot be demonstrated in all cases in which resection is performed. In so-called senile emphysema there may be extensive emphysematous changes that are in no way different from those of much lesser degree with bronchial obstruction, but there may be no evidence of bronchial obstruction. In all forms of emphysema there are found areas showing only merging of air spaces by traceless disappearance (atrophy) of partitions, and the air spaces so formed are abnormally large but not hyperinflated. In other areas there may be evidence of mechanical hyperinflation with disruption of partitions, compression, and displacement of adjacent lung areas. Here also there is usually evidence of local obstructive factors playing a role in their localization. It is well recognized that extensive emphysematous changes may remain clinically latent without obstructive manifestations, but the advent of obstruction makes much lesser degrees of emphysema clinically conspicuous. There is ample clinical and pathological evidence to show that air entrapment behind check valve obstruction does not satisfactorily account for more than the excessive hyperinflation of abnormal air spaces. Before this mechanical distention occurs, abnormal air spaces form by coalescence of normal air spaces by loss of partitioning, the essence of true emphysema.

In most recent literature indications now appear of beginning awareness of the problems of true emphysema. Churchill,[6] Head,[7] and Lengenhagen[8] have recently made important contributions to this. Describing observations on the physiological function of lung segments, Churchill discusses the nature of abnormal distention of air spaces in segmental lung areas and offers the concept of "space occupying function of air" as an answer to the problem of segmental emphysema. Head recognizes the fact that obstruction does not play the role generally attributed to it in the origin of emphysema itself and offers a new theory of pulmonary mechanics, explaining the development of emphysematous changes (cysts, bullae) by persistent expansion associated with loss of pulmonary elasticity. Lengenhagen contends that, even in presence of bronchial obstruction, the latter is not responsible for the distention of the affected air spaces. He attributes it to a hitherto unrecognized principle of pulmonary dynamics recently demonstrated by him. These concepts point up the complexity of the problem of diffuse emphysema and especially that of the origin of localized abnormal air spaces. In our opinion these concepts fall far short of solution, because they too look on emphysema as mechanical. The concepts advanced up to now are all based on the assumption that the lung structures behave like lifeless rubber.

Problem of the Common Denominator of All Air Space Abnormalities.—From the foregoing observations it is obvious that the ultimate problem is that of the primary factor in all air space abnormalities, including emphysema. The solution to this problem lies in a concept that can include all manifestations and can reduce them to a common denominator. There is need for a concept that will afford an explanation of localized bullous or cystic changes in otherwise normal lungs as well as diffuse pulmonary emphysema involving both lungs. Such a concept should explain on the same principle acute emphysematous changes of developmental or pathological origin as well as chronic diffuse pulmonary emphysema of undetermined origin (essential emphysema). It is our conviction that such a concept should be based on biological and not on mechanical principles of lung function. It is our belief that such a solution is available in our concept that looks on these changes as manifestations of air space disorder. If we accept this as a working theory, we may define air space disorder as a loss of air space partitioning due to lack of alveolar structure in lung defects of developmental or pathological origin. The normal expansion of the chest and lungs exerted upon such defects will result in air space disorder, that is, production of abnormal air spaces. Our concept implies that air space partitioning is part of the visceral function of normal lung structure. Therefore, air space disorder expresses a disturbance of the normal visceral function.

A full discussion of this truly biological concept of lung function is beyond the scope of this presentation. Suffice it to mention here that it was first proposed some years ago by one of us[9] and that a great deal of inferential evidence in physiological studies on lung function has accumulated since then that favors the existence of such a visceral function. A full discussion of the present status of this concept is planned for a forthcoming publication.

PRACTICAL ASPECTS

The practical implications of our concept exist chiefly in affording reasonable explanations for the clinical manifestations and a theoretical basis for new avenues of approach in treatment.

An outstanding clinical feature of air space disorder is its frequent presence without clinical manifestations when the roentgenographic evidence is most marked; contrariwise, it may be clinically most conspicuous when the roentgenographic evidence is discernible only with great difficulty. Localized air space disorder conspicuous by roentgenogram involving a large part of one lung or even both lungs may be present with little disturbance in the visceral function as a whole. In contrast, diffuse

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7. Head, J. R.: Observations of Mechanism of Emphysema and Surgical Treatment of Dyspnea, Quart. Bull. Northwestern Univ. M. School **25**: 210, 1951.
8. Lengenhagen, K.: Genese d. stenotischen Lungenemphysems, Schweiz. med. Wchnschr. **82**: 542 (May 17) 1952.
9. Miller, J. A., and Rappaport, I.: Relation of Pulmonary Function Fibrosis and Emphysema, Ann. Int. Med. **11**: 1644 (March) 1938.

air space disorder that is barely demonstrable by roentgenogram may involve both lungs as a whole and lead to severe disturbance of visceral lung function. Localized, as well as diffuse, air space disorders even involving extensive lung areas are for the most part well compensated for by available intact lung parenchyma, affording adequate visceral function. This compensatory function is, however, readily interfered with by bronchial obstruction which leads to mechanical hyperinflation of localized air spaces or by excessive bronchospasm, which depresses the efficiency of ventilation of compensating lung areas. Clinical observations indicate that such compensation eventually becomes associated with increased expansion of the chest and lungs and increased bronchomotor activity. With increasing air space disorder, as pulmonary insufficiency is approaching bronchospastic phenomena often become clinically manifest. Dyspnea supervenes as an expression of pulmonary insufficiency. The clinical picture then assumes asthma-like features, indicated in the term pseudoasthma. The medical treatment of clinically manifest air space disorder consists essentially of combating pulmonary insufficiency and bronchospasm and of keeping the airways open.

In the foregoing discussion it was shown that obstructive hyperinflation of lung areas affected by air space disorder is a frequent complication interfering with compensation of adjacent functioning lung areas.

Modern thoracic surgery now allows us to meet this situation by resecting lung segments so affected and making available functioning adjacent lung areas free for compensatory function. The prerequisite for such surgical intervention is, of course, an accurate estimation of the affected areas and the available functioning ones. The assessment of the extent of pulmonary involvement and of available functional reserve before surgery is most difficult and requires all examinations, including planigrams, angiograms, bronchograms, and double bronchospirometry studies. Long clinical experience and close cooperation between medical and surgical consultants is necessary.

SUMMARY

Clinical and pathological observations have shown that air space abnormalities described as cysts, bullae, and pneumatoceles are common and are probably increasing in frequency. They are practically always acquired in origin and are closely related to, or in fact are in the nature of, emphysematous changes in the lung. These observations have pointed up the need of explaining both abnormal air spaces that frequently show morphological features of developmental origin and the variable forms of air space abnormalities on the basis of prevailing concepts of emphysema. Our analysis indicates that current concepts do not afford an adequate explanation of these changes.

A new concept is proposed that looks on all these, including all forms of emphysema, as forms of air space disorder. This is interpreted as a disturbance of the visceral function of the lungs. The practical implications of this concept are briefly related.

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THE ESOPHAGUS IN GENERAL PRACTICE

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No specialist can claim the exclusive right to treat a specific organ or part of the body. The esophagus is no exception to this fact. The general practitioner, who almost always sees the patient first, is particularly aware of the importance of the proper interpretation of signs and symptoms. It is incumbent on every physician to be intimately conversant with the numerous manifestations that may be of esophageal origin. It is indeed embarrassing to misinterpret cardiospasm as coronary disease, to overlook a hiatus hernia as the cause of an "idiopathic" secondary anemia, or to consider the cyanosis of a newborn infant as due to a tetralogy of Fallot rather than a tracheoesophageal fistula. These errors are becoming less frequent as we learn more about the esophagus.

CARDIOSPASM

Cardiospasm is characterized by dilatation, hypertrophy, and tortuosity of the esophagus. Theories as to the cause of cardiospasm are numerous and nebulous and will not be discussed; however, it is sufficient to say that there is no known pathological origin of the condition. It is twice as common in women as in men, and in a large percentage of cases a history of emotional strain or psychic trauma can be elicited. Cardiospasm is the cause of 20% of all cases of dysphagia.

The outstanding symptoms are dysphagia, regurgitation, and retrosternal pain. Complete esophageal obstructions of varying duration, even to a point where the patient cannot swallow his own saliva, have been noted. Difficulty in swallowing is associated first with liquids and then with solids. The retrosternal pain varies from mild to severe, and prolonged use of morphine for relief may result in addiction to the drug.

Kramer and Ingelfinger have described the methacholine (Mecholyl) chloride test as an aid to the diagnosis of cardiospasm. When this parasympathomimetic drug is injected into normal persons there is only a slight increase in tone and magnitude of esophageal contractions. In patients with cardiospasm, however, marked esophageal spasm and contractions follow administration of the drug. Roentgenograms and esophagoscopy confirm the diagnosis. It is well to remember that in cardiospasm the esophagus is markedly dilated; in carcinoma it is moderately dilated; and in strictures it is mildly dilated.

Complications that may be associated with the condition are bronchitis, bronchiectasis, and pulmonary

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abscess, all of which can be caused by aspirated matter regurgitated from the esophagus.

Medical management includes use of psychotherapy, antispasmodics, and dilatation. Many surgical procedures have been advised, including cardioplasty, cardiomyotomy, resection, and anastomosis.

ESOPHAGEAL SPASM AND TENSE ESOPHAGUS

Esophageal spasm and tense esophagus are overlooked or misdiagnosed frequently. The condition is a functional derangement of the esophagus that is a somatic expression of psychic disturbances and is manifested primarily as an increase in muscular tonus in the absence of local organic pathology. It should not be confused with cardiospasm. Tonus is the muscular tension present in the noncontracting state or during diastole. Esophageal muscular tonus produces pressure in the lumen; hence this pressure varies according to the state of relaxation, and esophageal pain may be produced by increase of muscle tonus. Transit times can be temporarily slowed in some persons by emotional tension.

States of diastole involve different levels and have a wide range of severity. The term globus hystericus probably represents a mild increase in tonus in the upper esophagus. Patients with this condition should not be dismissed as neurotic but can be successfully and sympathetically treated. Tension states involving the midesophagus and the lower esophagus are associated with frequent belching, heaviness, and dull pain; these same symptoms are often mistaken as signs of gallbladder disease or gastrointestinal pathology. In the severe forms there is usually excruciating substernal or epigastric pain accompanied by dyspnea, pallor, sweating, and syncope. If these are erroneously associated with coronary disease an unnecessary cardiac cripple may result. It has been proposed that the term tense esophagus refer to increased esophageal diastole and that the term esophageal spasm be reserved for the more acute and severe attacks found in patients with a tense esophagus.

Every case of tense esophagus must be thoroughly investigated before a purely functional etiology is accepted. Overlooked cases of this type impress us with the truism —when the treatment does not work, do not condemn the therapy but suspect the diagnosis. General treatment for tense esophagus is the same as treatment of functional derangements elsewhere in the body. In severe or refractory cases medical therapy and bouginage almost always result in rapid and dramatic relief.

ESOPHAGEAL DIVERTICULA

Diverticula of the esophagus can be classified in two ways; by location and by structure. As to location, there are three locations, namely, upper (pharyngoesophageal), middle, and lower (epiphrenic). With regard to structure, if a section of mucous membrane herniates through the muscle layer it is a pulsion diverticulum, but if all layers of the esophageal wall are pulled to form the pouch it is known as a traction diverticulum. The so-called traction type is usually located in the region of the bifurcation of the trachea where chronically inflamed tracheobronchial lymph nodes are found. These diverticula rarely produce symptoms since they usually have a wide ostium that forms their neck. More important than classification is the pathological physiology, which explains the signs and symptoms. A weakness in the muscular wall is believed to be a prerequisite for a pulsion diverticulum. No symptoms are produced as long as the opening into the diverticulum is large.

As food slowly packs into the pouch it increases in size and drops downward. This process continues until the weighted diverticulum produces pressure on the esophagus, causing obstruction. It should be noted that in such fully developed diverticula food has easier access to the diverticulum than to the esophageal lumen. Dysphagia is the chief symptom and diverticulitis, perforation, and mediastinitis are common complications. Roentgenograms and esophagoscopy confirm the diagnosis.

In this day of chemotherapy, improved surgical technique, modern anesthesia, and proper postoperative care, the one-stage diverticulectomy is preferred to the two-stage operation. Diverticulopexy also has its place. This procedure in which the diverticulum is dissected free and is stitched upward to the surrounding structures is reserved for the poor risk patient who has symptoms. After the operation food does not have access to the hanging diverticulum, and the symptoms are alleviated.

ESOPHAGEAL VARICES (PORTAL HYPERTENSION)

A ruptured esophageal varix results from increased pressure in the portal system (intrahepatic or extrahepatic) and is almost always found at the lower end of the esophagus. The usual cause of intrahepatic block is cirrosis of the liver, and as long as cirrhosis continues to be a common disease esophageal varices will continue to be a threat to life. Extrahepatic block may be caused by phlebitis, thrombosis, fibrous stenosis, or cavernomatous transformation of the portal vein; it may be congenital or acquired. Differential diagnosis of gastroduodenal ulcer and an esophageal varix often challenges the physician's diagnostic ability. The cirrhotic habitus (the man with no hair on his chest) and the presence of gynecomastia and telangiectasia are often signs of liver abnormality. Banti's syndrome is characterized by splenomegaly, anemia, esophageal varices, ascites, and leukopenia. If the block is due to an intrahepatic lesion, results of liver function tests will be abnormal, whereas if the portal block is extrahepatic, results are usually normal. If the disease is in a quiescent stage it might be safe to take an esophagram, which would reveal the pathognomonic "beaded" appearance at the lower end of the esophagus.

Since hemorrhage from a ruptured esophageal varix may be rapidly fatal, definite measures must be taken to prevent a recurrence. Some of the therapeutic procedures advocated are injection of the varix with sclerosing agents, tamponade through the esophagoscope, ligation of the coronary vein, esophagogastric resection to remove the "diseased" area, and the various forms of portacaval shunts. This last procedure has become popular in the past few years, and various types of anastomoses intended to shunt the blood from the portal to the caval system have been attempted. More recently, splenic and hepatic artery ligations have been advocated.

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ESOPHAGEAL HIATUS HERNIA

An esophageal hiatus hernia is a type of diaphragmatic hernia in which the upper part of the stomach herniates through the esophageal hiatus. Three types of esophageal hiatal hernias have been described: the paraesophageal type, in which the stomach herniates through the hiatus and lies parallel to an esophagus of normal length; the sliding type, in which the stomach is herniated through the hiatus but has pushed an esophagus of normal length upward, rendering it tortuous; and the hiatal hernia with a congenitally short esophagus, in which the upper part of the stomach is herniated through the hiatus because the esophagus has never attained its normal length. The last type can be diagnosed by the appearance of gastric mucosa at an unusually high level. Hiatal hernias may be a coincidental finding in routine gastrointestinal roentgenograms. Such hernias rarely, if ever, produce any symptoms. Although many advocate no treatment, the danger of strangulation with resulting putrid empyema and rapid death is always present. On the other hand, many patients with hiatal hernias complain of epigastric distress, bloating, belching, anorexia, loss of weight, and retrosternal pain. Such cases have been diagnosed erroneously as gallbladder disease, peptic ulcer, gastritis, or coronary disease. These errors can be avoided if esophageal hiatus hernia is kept in mind, particularly if roentgenograms are taken with the patient in the Trendelenburg position, which would readily demonstrate an otherwise missed herniation.

Left phrenic nerve avulsion should always be considered, since it may relieve pressure and symptoms by relaxing the left side of the diaphragm. Surgical repair of a paraesophageal or a sliding type of hernia is simple, since all that is necessary is a reduction of the herniated stomach and tightening of the esophageal hiatus. Hernia with a congenitally short esophagus is the most difficult to treat successfully.

CONGENITAL DEFECTS

Much has been learned recently about congenital atresias and tracheoesophageal fistulas, so that they now can be properly classified and treated. Various combinations of these anomalies are possible. The most common defect is that in which the proximal end of the esophagus ends as a blind pouch and the distal end joins the trachea to form a tracheoesophageal fistula. Such a defect is suspected if the newborn infant has a symptom complex of coughing, choking, and cyanosis, especially with an abnormal amount of drooling and/or rhinorrhea. These cases should be considered emergencies, as the child may die of aspiration pneumonia. The roentgenologist may determine the type and site of such lesions by merely noting the presence or absence of gas in the stomach and bowel and by injecting a small amount of iodized oil (Lipiodol) through a nasal catheter into the proximal esophagus. Barium injections should never be used. If these few pertinent facts are kept in mind, every "blue baby" will not be considered to have a tetralogy of Fallot, and immediate and proper therapy can be instituted. Treatment of congenital esophageal defects is by surgery, and with modern methods a high percentage of cures can be expected.

CARCINOMA OF THE ESOPHAGUS

A defeatist attitude can no longer be assumed with regard to carcinoma of the esophagus. What was considered a hopeless and inoperable condition only a decade ago is now regarded as worth every effort. An early diagnosis is of paramount importance for increasing the survival rate in esophageal carcinoma. It may be said that any change in the swallowing habit that persists is a symptom of carcinoma of the esophagus until proved otherwise. If this dictum were followed and such symptoms further investigated by means of esophagoscopy and roentgenographic study, many esophageal neoplasms would be found and treated earlier.

Dysphagia is usually the first symptom, and the patient changes his eating habits progressively from steak to hamburger, to soft foods, and finally to liquids. There may be periods during which the patient believes the difficulty has passed. Although a tumor may involve a great portion of the circumference of the esophagus, symptoms may be minimal because of the distensibility of the remaining normal esophageal muscle. Pain and regurgitation are later manifestations. Esophagoscopy with biopsy is the only method by which a positive diagnosis can be made. The preferred treatment is surgical; irradiation therapy is of palliative value.

SUMMARY

The importance of being "esophagus conscious" has been stressed. Some common errors in diagnosis of esophageal conditions are discussed. When therapy fails to relieve a given condition one should doubt the diagnosis rather than condemn the treatment.

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Human Factors in Sanitation Programs in Africa.—In general the primitive African is very close to nature and the realities of life and death. Disease and misfortune are familiar experiences and come unaccountably like bolts from the blue. He feels that whatever stability and strength he has comes from the fact that he is part of a larger organism and that he can only preserve this modicum of power by playing most meticulously his special part in this organism. This attitude governs his whole life and results in extreme conformity to tradition, conservatism in thought and fear of innovation. In the absence of any general conception of the inherent nature of cause and effect, he regards the workings of fate as arbitrary and haphazard and, provided he has obeyed the traditional rules, he rarely blames himself for his failures or misfortunes, but is apt to attribute them to the anger of some external agency and believes himself bewitched. Since his rules of behaviour only apply within his group, and in relation to his clan land, and since he has no abstract codes, he is left without a guiding star when he leaves his tribal sphere. . . . The success of programs of social, health, or other development will depend largely on the degree of understanding with which the basic elements are presented to the African. In no field will this be more important than in that of environmental sanitation which, striking at the very root of his existence, whether in the tribe or in the rural or urban community in which he has made his life, may be most difficult for him to accept. Precipitate action must be avoided at all costs and a step-by-step approach developed. Yet the pressing fact remains that the future development of the continent may well depend to a large extent on the success achieved in raising environmental sanitation standards.—J. W. Wright, Some Human Factors in Sanitation Programs in Africa, *American Journal of Tropical Medicine and Hygiene*, July, 1953.

METABOLISM IN PARAPLEGIA

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and
W. James Gardner, M.D., Cleveland

The paraplegic patient often has been dismissed as one of the unfortunate by-products of war or accident and thereby often has been the victim of neglect and ignorance. The large number of persons with paraplegia resulting from World War II injuries necessitated establishment of paraplegia centers where patients were rehabilitated as fully as possible. It soon became evident that the primary problems in these long-term patients were directly related to metabolic changes caused by their condition. Many of these changes had been noted in paraplegic patients in civilian life, but the small opportunity for study of large groups of patients often prevented the development of thought and investigation of these problems.

In recent years there has been widespread reemphasis and realization of the importance of metabolism and its changes. It has been found that many of the metabolic changes heretofore apparently limited to the paraplegic person are nonspecific changes that may be produced by any form of trauma. While paraplegia is commonly accepted as being of traumatic origin, functional transection of the spinal cord caused by disease or illness results in a similar pattern of metabolic change.

In this paper metabolic changes in paraplegic patients are examined in the light of recent knowledge, with the hope that better understanding of these changes will lead to more successful management. Occasional reference is made to specific cases, seen in the neurological surgery department of the Cleveland Clinic, to illustrate certain metabolic changes and their consequences.

CLINICAL COURSE OF PARAPLEGIA

The neurological changes occurring in the course of recovery from transection of the spinal cord may have little direct metabolic consequence; however, the resultant neurophysiological changes may have much to do with the alteration or aggravation of the metabolic changes. Riddoch,[1] in his classic description of the reflex activity of the paraplegic patients in World War I, included as the last stage in the clinical course the stage of gradual failure of reflex activity brought about by toxic febrile complications. Kuhn,[2] discussing patients of World War II, does not acknowledge the existence of such a stage. Such have been the advances in the knowledge of the paraplegic person and his metabolism. The present concept of the clinical course of paraplegia includes the following stages.

Stage of Flaccidity.—This stage is characterized by complete suppression of reflex activity below the level of spinal cord injury by "spinal shock," decreased myotatic irritability, dry skin easily made erythematous by pressure or scratching, distention of the bowel and retention of urine, and rapid heat loss from the denervated area. "Spinal shock" is the period of reflex suppression, which may vary considerably, from the condition of acute traumatic shock to the more subacute and even chronic periods of metabolic change. This period averages six weeks after the initial transection of the spinal cord, until there is evidence of returning reflex activity. A few cases of a much more prolonged period of "spinal shock" have been recorded,[2] and in several of the cases seen at the Cleveland Clinic the "spinal shock" period was from six to eight months long. During this period certain metabolic changes may be profoundly altered or may fail to reverse to normal as long as "spinal shock" continues.

The period of metabolic shock that follows acute transection of the spinal cord is a definite period during which profound body changes may occur. The term "shock," however, is rather general and may mean either traumatic or surgical shock, "spinal shock," or the acute shock phase of the alarm reaction of Selye.[3] The first stage of his general adaptation syndrome is the alarm reaction, which in turn is characterized by the shock phase and the subsequent countershock phase. The shock period discussed here, varying from a few minutes to 24 hours, in general corresponds to Selye's shock phase. Transection of the spinal cord in experimental animals has been shown to produce a typical alarm reaction, although the environmental temperature may mitigate the response.[4] Complete absence of symptoms of the alarm reaction may be possible if the body temperature is maintained by artificial means. When it is not, there is a characteristic drop in the body temperature.[5]

In the shock phase there is an acute vasodepression period, which may never advance to the surgical shock level if good nursing care is maintained. There is evidence of impaired circulation resulting from marked reduction in the total number of red blood cells, the hemoglobin, and the red cell volume, and a slight reduction in the total blood volume.[6] Varying degrees of hemoconcentration may make these changes less evident.[3] The causes of these changes include trapping of the red cells in the capillaries, an increase in the plasma volume, an increased red cell destruction of indefinite etiology, and retardation of hemopoiesis due to the fall in blood pressure and in spite of the stimulus of decreased oxygen tension. The blood clotting time shows a definite decrease, with an equal acceleration of fibrin formation. The platelet count rises, as does the globulin content of the plasma, at the expense of the albumin content.[7] These circulatory dynamic changes are not as profound as those seen in other types of trauma because of the lack of certain nervous factors furnished by the intact spinal cord.[8] The latter are not deleterious nervous impulses but are normal functions of the nervous system in response to an alarm stimulus.[9]

There is a general depression of cellular metabolism with a fall in the basal metabolic rate roughly propor-

From the Cleveland Clinic and the Frank E. Bunts Educational Institute.

Because of lack of space, the bibliographic references have been omitted from THE JOURNAL and will appear in the authors' reprints.

tional to the degree of the shock, although the respiratory quotient rises.[10] Some of the factors responsible are anemia, hypoxia, pain, and the loss of body heat. Nitrogen metabolism shows an early retention, but the nitrogen balance soon becomes definitely negative due to the catabolic effect of the shock phase. The blood urea, amino acids, and polypeptides likewise show early retention. Urinary excretion of creatine is augmented, although the blood creatine rises.[11]

There are similar changes in electrolyte metabolism. The potassium content rises in the blood and tissue fluid because of cell destruction and shows a similar increase in the urine. There is a pronounced decrease in the blood chlorides and in the chloride content of the tissues in general, although the chloride content of the brain and the muscles usually increases considerably above the normal level. Blood sodium decreases according to the chloride fall, as does the urinary excretion of chlorides. Blood phosphate level is elevated during the shock phase.[12] The change in carbohydrate metabolism is reflected by elevation in the blood sugar. Ketone bodies in the blood also increase. There is decreased sensitivity to the effects of insulin.[13] Fat metabolism shows little change except the frequent appearance of lipid deposits in the liver from immobilization of portions of the peripheral deposits.[14]

The mechanisms underlying these rapid changes in metabolism are incompletely understood at present. It is believed, however, that the alarm stimulus or damaging agent (perhaps through a hypothetical toxic metabolite produced under its influence) acts on the anterior lobe of the pituitary and stimulates it to discharge adrenotropic hormone. This in turn stimulates the adrenal cortex to produce an excess of corticoid hormones, which helps raise the resistance of the body and elicits the characteristic phenomena of the alarm reaction. These changes bear a striking similarity to those elicited by an overdose of adrenocorticotropic hormone.[14]

Return of Reflex Activity.—These stages in the clinical course of paraplegia advance from the return of minimal activity of the superficial genital reflexes, through varying degrees of flexor activity, to a pronounced degree of extensor activity. After the immediate responses of the body metabolism to the trauma of spinal cord transection, as characterized by the shock phase, there is a reversal of many of these responses. Selye[3] terms this the countershock phase. As the body tends to counteract the trauma and build up resistance, the countershock phase gradually merges into the stage of resistance, the second stage of Selye's general adaptation syndrome, and specific resistance reaches its peak. This period of the building of resistance will be discussed in considering the postshock period.

During this period the body temperature rises 2 to 3 degrees F, paralleling the increase of nitrogen in the urine. There is blood dilution with an increase in the total blood volume, often to a level above normal. Diuresis may occur.[3] The most profound change is an abnormal loss of nitrogen. The peak loss occurs in from four to eight days.[11] Electrolyte changes occur with an early hyperchloremia in the countershock phase. Potassium is retained to some degree, although the blood level and urinary excretion are high. The peak excretion occurs in from three to four days. The blood sugar, which may have fallen if the shock phase was prolonged, rises during the countershock phase and may reach hyperglycemic levels even if there has been no food intake. These levels may exceed the renal threshold and glycosuria will occur.[3]

EFFECTS OF IMMOBILIZATION AND BED REST

One of the best treatments for an ill patient is bed rest, but in many cases it eventually may do more harm than good. The paraplegic patient is as likely a candidate for prolonged bed rest as any; however, he derives great benefit from early ambulation.

In a study of normal, healthy young men immobilized in plaster casts from the waist down, Deitrick, Whedon, and Shorr [15] found definite changes in the body metabolism. There was a progressive nitrogen loss, starting on the fifth to sixth day after immobilization and reaching its peak in from 10 to 12 days. The urinary excretion of potassium, phosphate, sulfur, and sodium increased in a proportion correlated to the amount present in muscle and correlated to the amount of urinary calcium excreted. Calcium content in the urine was doubled, and calcium in the feces was variably increased. Creatine tolerance decreased with a corresponding decrease in the mass and the strength of the immobilized muscles. The basal metabolic rates fell an average of 6.9%. Exercise tolerance was decreased, and there was a consistent elevation of the pulse rate.

The chief cardiovascular deficits that appear on immobilization are reduction in the total blood volume and a lower peripheral venous pressure with postural hypotension. The average loss in blood volume varies from 5.4 to 9.3% in several studies, or about 500 cc. for the average person.[16] Some of this volume decrease is explained by a contraction of the plasma volume, which averages 15.5%.[17] The lower venous pressure is probably attributable to a reduction in the venous return and cardiac output that cannot be overcome by function of the natural moderator reflexes. Exactly which of the several vasopressor mechanisms is at fault is uncertain.[16b]

In the normal breakdown and repair of the body tissue, there is a continual removal and replacement of collagenous fibers. In the subcutaneous tissue, around joint capsules, in muscle planes, and in other similar locations, collagen is laid down as a loose, areolar, connective tissue that allows considerable range of motion among the moving parts. During immobilization and bed rest, however, there is shortening and tightening of the connective tissue as it is laid down. The collagenous fibers form a dense, hard scar or contracture, and this fibrosis causes loss of joint mobility. The rate of replacement is not known, but there is evidence that gross changes in deposition occur in from four to five days. By the end of three weeks the collagen scar may be extremely strong, and resumption of joint mobility may be exceedingly difficult. Thus, a cycle of immobilization may be the end-result.[18]

PROTEIN METABOLISM

The importance of protein metabolism is almost self-evident, because protein is one of the most important materials of the cellular protoplasm and next to water is the most abundant body constituent. Since the primary end-products of protein metabolism in the human

body are the nitrogenous waste products composed chiefly of urea, the so-called nitrogen balances are used as indices of protein metabolism. The difference between the nitrogen taken in the food and that excreted in the feces and the urine is spoken of as the nitrogen balance. When the intake and the output are equal the body is said to be in nitrogen equilibrium. When the intake exceeds the output the body is in positive nitrogen balance; when the output exceeds the intake the body is in negative nitrogen balance.

The healthy adult requires protein to replace the inevitable loss of tissue protein. If the diet contains protein in excess of the amount needed to repair "wear and tear," the nitrogen not employed for repair is excreted, and nitrogen equilibrium is maintained. In starvation, on a low protein diet, and with trauma in general, a person continues to excrete nitrogen derived from the dissolution of his own protoplasm and so goes into negative balance.[19] The significance of the nitrogen equilibrium may be misinterpreted, however, when applied to the ill, if it is used as an absolute scale of a normal protein status. As the body is deprived of adequate protein intake, its protein and caloric needs are correspondingly reduced. With each daily loss of protein and further reduction of tissue mass, an increasingly lower protein and caloric intake is required to attain equilibrium. The equilibrium reached at such a low level of intake is more indicative of hypoproteinia than of normoproteinia, and ease of attaining equilibrium may be used as a means of detecting hypoproteinia.[20] Daily nitrogen excretion of a man of average weight on a nitrogen-free diet is about 3 gm. It might be thought that nitrogen equilibrium can be reestablished by simply feeding the patient this quantity of protein nitrogen. A considerably larger quantity must be fed, however, because the amino acids required by the body are usually in different proportions than those found in the food protein. Certain electrolytes are necessary, also in proportions. Thus a relatively large food assortment must be available and must also contain the other two food principles, fats and carbohydrates, since with an exclusively protein diet it is impossible to achieve nitrogen equilibrium because of the body's energy requirements.[19]

The postshock period of protein metabolism is characterized by the loss of nitrogen. In the first two weeks after spinal cord transection the greatest nitrogen loss occurs, directly in proportion to the severity of the injury to the spinal cord. The peak loss takes place in from three to six days and may reach a maximum of from 22 to 29 gm. of nitrogen per day. From two weeks after transection until about six months later, the degree of nitrogen wastage and its duration depend upon the severity of the initial catabolic response and the patient's ability to recover. If positive nitrogen balance has not been achieved after the six month period, the patient will be chronically debilitated, with little chance for survival.[19] The average period of nitrogen loss, as evidenced by the elevated urinary nonprotein nitrogen, is from 30 to 45 days if there has been some return of the reflex activity within this period. Most of the increased urinary nonprotein nitrogen is in urea and ammonia, with a slight increase in creatine.[21]

In poliomyelitis patients with bulbar-spinal or spinal involvement and extensive paralysis, the 24 hour urinary nitrogen excretion has been found to be the single most reliable index of the catabolic process and of the transition to other phases. Patients in hypotensive shock with decreased renal output are the exception to this generalization.[22] During the catabolic period there is a fall in the serum albumin and a rise in the serum globulin. In poliomyelitis patients this reversal of the serum proteins appears to have a direct relationship to the duration and magnitude of excessive protein destruction and the severity of the disease.[23]

The catabolic process apparently is involved in the transport of protein and minerals from the body stores to the wound site, but this is hardly true in the case of immobilized normal persons, who show the same catabolism. Debilitated patients also fail to show an increase in urinary nitrogen excretion. This failure to show a catabolic reaction might be explained on the basis of acquired resistance to nonspecific trauma of long duration. It may also be explained on the basis that debilitated persons have little storage protein. Evidence indicates that some part of the cellular protoplasm is storage protein that the cells can yield without effect on their viability and that the excessive nitrogen output may arise from this storage protein rather than from essential tissue substances.[24]

Many investigators have thought the period of negative nitrogen balance is an irreversible stage, because studies have shown that with an oral intake of protein up to 100 gm. per day practically the entire nitrogen content of the protein is excreted as urea within 24 hours. Nitrogen of intravenous protein hydrolysate is utilized in much the same manner as food nitrogen, but the nitrogen of intravenous plasma does not appear in the urine. Presumably all of this protein intake is used for energy purposes and not anabolism.[25] Recent investigation, however, has refuted this concept of irreversible catabolism. If an adequate caloric intake of about 50 calories per kilogram of body weight and high protein feeding, about 500 gm. per day, are used, positive nitrogen balance can be achieved and maintained throughout the entire postshock period. Certain special methods of nutrition are often necessary to achieve this high level of feeding.[20]

During the period of catabolism, fever plays only a small role in the nitrogen loss, but infection may play a large role. The problem of infection is of particular importance in the paraplegic patient, because he is susceptible to sepsis in the genitourinary tract. Atrophy of the paralyzed extremities from disuse contributes only a small part to the nitrogen loss. In the early stage of convalescence the positive nitrogen balance may be temporarily returned to a mildly negative balance by light exercise or by fatigue.[26]

ELECTROLYTE METABOLISM

Potassium, the chief basic ion of the body cells, is the most important inorganic substance in the group of electrolytes. The body of the average adult contains about 175 gm. of potassium, all of which is in the cells except for about 11 gm. divided among the extracellular spaces, blood cells, and the blood plasma. Trauma results in

cellular breakdown, as shown by the development of negative nitrogen balance. For every gram of nitrogen broken down, about 2.7 mEq. of potassium is released. This released potassium is added to the urinary excretion of the cation. The ratio of urinary excretion of potassium to that of nitrogen is about 1 to 10. The peak loss of potassium will usually occur in from three to four days after trauma.[28]

For the fabrication of protein it is necessary to have all of the essential components of the particular tissue, which means that, in addition to the required amino acids, the necessary inorganic salts, particularly potassium, must be available. Experiments in animal feeding have shown that amino acid preparations that were nutritionally adequate in the amount and the distribution of usable nitrogen produced poor growth when diets deficient in potassium were used. This seems to indicate that a minimal daily intake of potassium is necessary in the process of protein repletion.[27]

After the immediate postshock period little change takes place in the sodium and chloride metabolism, unless there is some complicating factor that produces electrolyte loss, i. e., vomiting or diarrhea. The pathological effects of potassium deficiency may be materially modified by restriction of the sodium chloride intake, for as the sodium chloride intake rises the effects of potassium deficiency increase. Alterations in sulfur metabolism parallel those of protein metabolism. Sulfur is present in the body largely as a constituent of two amino acids, since the body does not utilize inorganic sulfur in manufacture of body protein. The ratio of sulfur excretion to nitrogen excretion is about 1 to 14 gm. Thus, during the period of negative nitrogen balance, the urinary excretion of sulfur is high. During protein anabolism a minimal daily intake of sulfur is necessary for protein production. This is furnished if the diet contains the necessary amino acids.[28]

CALCIUM AND PHOSPHORUS METABOLISM

Alterations in calcium and phosphorus metabolism are largely caused by the bone changes that occur as a result of the immobilization and bed rest. Although bone is rigid and seemingly permanent, it is really a dynamic tissue that is broken down and rebuilt continuously. Local stress and strain dictate the areas where new bone must be built. In the absence of stress and strain there is a decrease in the activity of the osteoblastic cells. The decreased formation of the organic matrix, but with a continuation of the normal osteoclastic activity of bone resorption, leads to demineralization and osteoporosis. The mechanisms for the homeostasis of calcium and phosphorus in the blood remain the same; hence they are present in normal amounts in the serum but are definitely increased in the urine. The amount of ionized calcium usually increases with recumbency.[29] The hypercalcinuria and hyperphosphaturia exist for at least the first 60 days after immobilization. The excretion level stabilizes after about 30 days and may remain so until mobilization occurs.[30]

HORMONE METABOLISM

The characteristic pattern of metabolic response to trauma is largely set by hormonal action. As mentioned before, the theoretical chain of events is from pituitary stimulation to adrenal cortical outflow, since many of the changes bear a striking similarity to those elicited by an overdose of adrenocortical hormone.[13a] Exposure to stress increases the tissue utilization of adrenocortical hormone, thereby decreasing the effective blood level that activates the anterior lobe of the pituitary to elaborate the adrenocorticotropic principle. The adrenal cortex and its secretions are particularly responsible for the control of protein metabolism and the excretion level of the urinary nonprotein nitrogen. Administration of these hormones in excessive amounts can cause an increase in the urinary nitrogen excretion; however, in animals in which the adrenals are replaced by a constant dose of cortical extract, trauma is attended by the same nitrogen excretion. Thus no increased adrenal secretion is necessary. For 24 to 48 hours after trauma, the urinary output of 17-ketosteroids is increased; then it falls below normal levels for a period approximating that of the catabolic reaction. Secretion of urinary cortin-like substances is increased for the same length of time. Perhaps the necessity of the presence of adrenocortical hormones for the protein metabolic response is based upon the potentiation of the thyroid gland in its control of nitrogen, since an increase in urinary nitrogen excretion results from the administration of thyroxin, an amino acid of the thyroid. A hormonal cause for the failure of debilitated patients to show a catabolic reaction is suggested by the fact that chronic underfeeding in rats produces a pseudohypophysectomy.[21]

COMPLICATIONS AND THEIR METABOLIC RELATIONSHIP

Decubitus Ulcer.—The decubitus ulcer is a common complication of paraplegia and can be one of the most distressing problems in the patient care. The incidence of ulcers in paraplegic patients varies from 95% in war cases to 28% in civilian cases.[31] Poer [32] found that 57% of war injury paraplegic patients at general hospitals in the U. S. had decubitus ulcers. The incidence of ulcers in paraplegic patients at the Cleveland Clinic during the past six years was about 46%.

Munro's theory [33] on the etiology of the decubitus ulcer is that the prolonged pressure on a single point leads to local tissue anemia. The normal skin maintains the vascular reflex, bringing more blood to the periphery of the pressure point. There is an absence of autonomic reflex function as well as somatic reflex function in the stage of "spinal shock," and after recovery of reflex function there is always some impairment in the functional efficiency of the autonomic responses, particularly those of pilo-erection, sweating, and vasomotor tone.[34] This autonomic impairment is further evidenced by the fact that in about 54% of the paraplegic patients with decubitus ulcers the spinal cord lesion is in the thoracolumbar area where the autonomic centers and outflow are concentrated. The ulcers are found in 20% of patients with lesions of the cervical cord and in 18% with lesions in the cauda equina.[31b] Since there is no increase in oxygen-bearing blood to the pressure point, local anoxia soon results, leading to local tissue necrosis.[33]

In addition to the local tissue changes, the factors of protein depletion and anemia are paramount in development of the decubitus ulcer. In Poer's series of paraplegic

persons with ulcers, the majority had a negative nitrogen balance, and at least 74% had moderate to severe anemia.[32] Mulholland [35] reports that in a series of unparalyzed patients with negative nitrogen balance all decubitus ulcers healed when the catabolic state was reversed. Once a decubitus ulcer has developed, it will further aggravate and perpetuate the catabolic state by causing the loss of as much as 50 gm. of protein per day. Thus it is evident that protein anabolism must be achieved for satisfactory healing of the decubitus ulcer.

Anemia and Hypoproteinemia.—Anemia and hypoproteinemia often are the two most evident clinical manifestations of serious metabolic alterations in the paraplegic patient. Although there is considerable interrelationship in their metabolism, each disorder may exist totally independent of the other. The nutritional status of the paraplegic patient may have as much to do with the metabolic disorders as does the trauma itself. In Poer's survey, 74% of patients showed a serious loss of body weight averaging 42.5 lb. (21.25 kg.) per patient. The severe mental depression that many of these patients exhibited, with its resultant anorexia, was added to the inevitable changes in the protein metabolism. A moderate to severe secondary anemia was present in 74% of the same group of patients. In the absence of a significant degree of blood loss these severe anemias may be difficult to explain completely.[32]

In addition to the nutritional status and the protein catabolism, defects in iron metabolism may be brought about by impaired liver function in the acute shock and early postshock periods. The rate of blood regeneration following blood loss has been shown to depend chiefly upon the available body stores of iron, which, when depleted, are replaced slowly. Although iron is stored in many tissues, including the spleen, bone marrow, and the kidneys, the main storage depot is the liver. The mechanisms of iron metabolism in the presence of impaired liver function have been incompletely studied, but it is accepted that aplastic anemia may occur with liver disease.[36]

Hypoproteinemia is not necessarily present when the body has a protein deficiency. It has been shown that plasma proteins remained within the normal range even when there was a 25% loss of the body weight after a prolonged period of semistarvation and in the presence of symptoms of hypoproteinia such as reduced organ size, alterations in the fluid compartments and in tissue permeability, and mental changes.[20] In hypoproteinemia, for each gram of plasma protein that is lost there is an accompanying loss of 30 gm. of tissue protein. Thus, in an average size man weighing 140 lb. (70 kg.), with the loss of 1 gm. per hundred cubic centimeters in the plasma proteins, about 1,030 gm. of tissue protein are lost. These same relationships apply to the regeneration of protein during anabolism. Approximately 3.5% of the available nitrogen goes into the serum albumin and the remainder to the tissue proteins. There is relatively little change in the plasma albumin level after large doses of protein, a fact that has been too frequently forgotten in the clinical treatment of protein deficiency. In the presence of anemia the available nitrogen will first be diverted to the synthesis of hemoglobin, at the expense of tissue protein regeneration. It is extremely important to correct the anemia first by the use of whole blood.[37]

Liver Function.—Some degree of liver function impairment is a consequence of trauma, such as war wounds and surgical operations, and is particularly noted after spinal cord transection.[38]

In tests for liver function there is a definite retention of sulfobromophthalein (Bromsulphalein) sodium that may amount to as much as 18 to 40% during the first two weeks after spinal cord injury.[10] The abnormal results do not appear to be related to elevation of body temperature, loss of blood, severity of the post-traumatic catabolic reaction, or to the level of the lesion in the spinal cord. There does appear to be some relationship between the degree of retention and the severity of the injury to the spinal cord.[39] Normal function usually returns within three to six weeks if the patient is going to recover. Early ambulation has no influence on the return of normal liver function.[40] The urinary excretion of urobilinogen increases abnormally during the same period in which sulfobromophthalein retention occurs. Return of the urobilinogen level to normal parallels the sulfobromophthalein changes and is unaffected by ambulation.[38b]

The mechanism of impairment of liver function is indefinite, but it appears to be one of the many organ changes of the post-traumatic catabolism. Selye [3] describes some cloudy swelling of the liver cells and a decrease in the blood volume of the liver during the alarm reaction. Impairment of liver function has not been completely investigated, but it may be an important factor in metabolic changes such as protein catabolism and iron metabolism. It may also contribute to permanent liver changes, such as hepatomegaly and amyloidosis,[45] occasionally noted in paraplegic patients.

Bone Changes.—The paraplegic patient frequently has abnormal changes in the bones or the adjacent soft tissues in the paralyzed portion of the body. These changes are caused partly by abnormal local stimuli or the lack of stimulation and partly by the body's response to abnormal metabolic changes.

One important bone change is erosion, which is evident in 45% of paraplegic patients. Eighty-five per cent of the patients showing these bone changes also have decubitus ulcers, because there is a direct relationship between the bone and skin lesions. Bone lesions tend to develop wherever the soft tissue over a bony prominence becomes devitalized. Biopsies show subacute and chronic infection of the tissue overlying the bone with extension of the infection into the superficial layers of bone. This leads to resorption of the cortex and the underlying trabeculae, and the marrow is replaced by fibrovascular tissue. These changes are evident roentgenographically first as loss of the cortex and later as a rough, shaggy appearance of the bone surface. There is erosion and flattening of the prominences. With early repair, reshaping or molding of the prominences occurs, and, with later repair, proliferation leading to abnormal contours occurs. Joint surfaces are not involved.[42] The other important bone change is generalized osteoporosis in the paralyzed

portions of the body. This is a disuse phenomenon caused by immobilization and is present in varying degrees in every paraplegic patient.

The soft tissue change of abnormal ossification occurs in about 43% of paraplegic patients and may occur rarely in a patient with a traumatic cord lesion in which function will return. All patients showing ossifications have or have had decubitus ulcers, but there is no correlation of areas that are involved by the two types of lesions. Ossifications are most frequently found near one of the larger joints, such as the hip or knee joint. Ossifications may occur in the muscles, tendons, tendon sheaths, ligaments, and joint capsules, or may be attached to the periosteum. The periosteum adjacent to ossifications shows no changes, as ossifications do not affect or arise from the periosteum. They usually form in a few weeks to several months after the injury and assume a mature trabecular pattern that tends to remain constant in roentgenographic appearance.[43] The cause of these abnormal ossifications is indefinite. Local injury with hematoma formation may explain part of the change. A neurogenic factor is involved, because these lesions are never seen above the level of the spinal cord lesion and are rarely seen in patients showing functional return of spinal cord activity. There is probably some abnormal tissue response to the altered calcium and phosphorus metabolism. Although blood calcium and plasma protein contents are the same in patients with and without the ossifications, blood phosphorus and phosphates are significantly elevated in patients with ossifications.[43a]

The effect of ambulation on these abnormal bone and soft tissue changes is profound. In a series of paraplegic patients, 12% of ambulant patients showed a mild osteoporosis, while 83% of nonambulant patients had a more severe osteoporosis. There was a 12% incidence of soft tissue ossifications of a minimal degree in ambulant patients compared to an incidence of 47% of ossifications to all degrees in nonambulant patients.[44]

Renal Changes.—The genitourinary tract is particularly susceptible to pathological alterations as a result of some of the metabolic changes and changes in the neurophysiology of the bladder due to the spinal cord lesion. Riddoch's third stage in the clinical course of paraplegia, that of decreasing reflex activity due to toxic febrile complications, was primarily based upon genitourinary sepsis.[1] Better understanding of the pathophysiology of the neurogenic bladder and use of chemotherapeutic and antibiotic agents have eliminated Riddoch's third stage from the modern concept of the clinical course of paraplegia. In World War I there was an overseas mortality of about 80% in the spinal cord injury cases, and, of these, 47% were due to genitourinary complications. In World War II there was an overseas mortality of 12%, and, of these, 1.5% were due to genitourinary complications.[45]

The most important metabolic changes that affect the genitourinary tract are those of calcium and phosphorus content. The hypercalcinuria present in all nonambulant paraplegic patients remains throughout the period of immobilization. In the immobilized patient there is usually an increase in the ionized calcium. Lowered plasma protein with normal blood calcium level causes an increase in the proportion of ionized calcium to protein-bound calcium. This increases the amount of ionized calcium available for stone formation. The recumbent position of the patient causes accumulation of sediment in the renal calices, furthering the tendency toward stone formation.[29] Renal calculi in spinal cord injuries of all types vary in incidence from 10 to 20% in different series of cases. Bladder calculi in the same series of cases vary in incidence from 20 to 70%.[45]

Various methods of diminishing the concentration of calcium in the urine, such as forcing fluids, acid ash diets, elimination of milk and fruit juices in the diet, and elevation of the head of the bed, have been advocated. The best prophylaxis is ambulation, which decreases hypercalcinuria almost immediately.[46]

Endocrine Changes.—Hormonal changes, which are an integral part of the body's response to the trauma of spinal cord transection, may have some profound effects upon the various endocrine systems and sexual functions of the body. The roles of hormonal change and of neurogenic factors after the spinal cord section have not been adequately defined. Selye [3] postulates that atrophy of the gonads of both sexes is caused by a shift in the hormone production of the pituitary, increasing the output of the adrenotropic hormones at the expense of the gonadotropic hormones.

Cooper, studying a series of paraplegic men, found that testicular atrophy occurred in over 50%.[47] Testicular biopsy studies have shown that there is arrested maturation of the germinal epithelium in at least 62% of the cases. The testicular changes had no relationship to local infections (epididymitis), duration of the spinal cord lesion, general systemic factors, degree of sexual potency, or the level of the cord lesion between C_6 and L_5. The factors of denervation of the epithelium and tropic changes secondary to the vasoparalysis of the spermatic cord and testicular vessels are possible explanations.[48]

Little study has been made of endocrine changes in paraplegic women because of the rarity of such patients. Young adult women with post-traumatic paraplegia usually cease menstruating for three to six months after injury, and subsequent flow is scanty and irregular.[39] Similar changes have been observed in patients seen at the Cleveland Clinic. In a young adult woman with paraplegia resulting from a degenerative spinal cord disease (neuromyelitis optica), menstruation did not resume until 18 months after the onset of paraplegia.

Gynecomastia has been observed in 22 to 25% of paraplegic men. No consistent endocrine abnormality has been demonstrated as the cause.[49]

SUMMARY

The present knowledge of metabolic changes in paraplegia is presented. Many of these changes are not limited to the paraplegic patient but occur as definite and consistent reactions to trauma of any form. Some specific complications of paraplegia are discussed, with emphasis on the metabolic abnormalities that underlie them. No attempt is made to discuss treatment of metabolic alterations, but the basic facts on which effective treatment depends are presented.

INCIDENCE AND CLINICAL MANIFESTATIONS OF CARDIAC METASTASES

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The incidence found at autopsy of cardiac metastases in patients who died of cancer is reported in the literature to be less than 4%.[1] Pollia and Gogol [2] found involvement of the heart by metastatic disease in 29 cases among 1,450 autopsies of patients dying of cancer; Scott and Garvin,[3] 101 among 1,085; Ritchie,[4] 16 in 857; and Prichard,[5] 146 of 4,375 cancer autopsies. The disproportionate frequency of serial changes in the electrocardiograms of patients dying of cancer at Memorial Center led us to review the clinical and postmortem data of 500 consecutive cancer deaths observed between 1948 and 1950.

METHOD AND MATERIAL

The incidence of cardiac metastases in the various neoplastic diseases encountered was tabulated, and the exact site of the metastases, as well as the degree of cardiac involvement, was noted. The clinical, electrocardiographic, and roentgenographic findings were correlated, insofar as possible, with the pathological changes described at autopsy. No primary heart tumors were encountered in this series, and therefore discussion of these rare tumors will not be included. Data are based on 124 patients dying of leukemia, 69 of lymphoma, and 307 of other tumors. For the purposes of this study we include under the heading of lymphoma the following conditions: Hodgkin's disease, Hodgkin's sarcoma, Hodgkin's granuloma, lymphosarcoma (all types), and reticulum cell sarcoma. The leukemias were represented by acute and chronic lymphatic, acute and chronic myelogenous, acute monocytic, acute micromyeloblastic, and stem cell leukemia.

RESULTS

The over-all incidence of cardiac infiltration in 119 patients with leukemia of various types was 44% (52 patients). A slightly greater frequency of myocardial infiltration was noted in lymphatic leukemia (58%) than in myelogenous (40%). In acute myelogenous leukemia, occurring in 53 persons, the incidence was 42% (22 patients with cardiac involvement) as opposed to 35% (7 of 20 persons) in the chronic form, and the incidence was 59% (10 of 17) and 57% (8 of 14), respectively, for chronic and acute lymphocytic leukemia. Cardiac infiltration was found in 23% (3 of 13) of patients with stem cell leukemia and in the one patient each with acute monocytic and acute micromyeloblastic leukemia. No postmortem evidence of cardiac involvement was found in five patients with multiple myeloma. The cardiac involvement in all instances was characterized by interstitial and perivascular infiltration of the heart with leukemia cells. Occasional microscopic areas of fibrosis and myocardial necrosis were encountered.

The frequency of cardiac infiltration in 69 patients who died from lymphomas of various types was established, with an over-all incidence of 24% (17 patients). No significant differences were found among Hodgkin's disease (29%, or 4 of 14), Hodgkin's sarcoma (31%, or 4 of 13), and reticulum cell sarcoma (30%, or 7 of 23). Cardiac infiltration was found in only 13% (2 of 15) of the patients with lymphosarcoma and in none of the four cases of Hodgkin's granuloma. The type of involvement was variable in extent. Tumor cells were seen in epicardial fat, often extending into and between underlying muscle fibers. At times, massive replacement and destruction of muscle were noted.

In table 1 the incidence of cardiac metastases from visceral and cutaneous tumors is presented, with an over-all metastatic rate of 12%. These 304 patients had 62 types of malignant tumors. Cardiac metastases were found in 37 instances in 152 autopsies, representing 15 different types of neoplastic disease. In the remaining 155 patients (47 tumor types) the heart was not involved. The three commonest tumors producing cardiac metastases were carcinoma of the lung, carcinoma of the breast, and malignant melanoma. The incidence of cardiac involvement in the 12 other types of tumors varied widely and is also listed in table 1.

Three of the five patients with malignant melanoma had cardiac metastases. Scott and Garvin [3] reported cardiac involvement in 5 of 10 such patients (50%), and Moragues [6] in 4 out of 7 (57%). This high incidence, together with other reports, prompted us to augment the series by studying additional autopsies of patients who died with malignant melanoma at Memorial Center and a series of private patients collected by Dr. George T. Pack, totaling 34 in all. The distribution of metastases in these 34 patients is presented in table 2, with 15, or 44%, showing cardiac involvement. In no instance was the heart the sole site of metastases, and in almost every instance when the heart was involved widespread metastases were present elsewhere as well.

Similar data are listed in table 3 for 106 patients with cardiac metastases resulting from tumors other than melanoma. The distribution of the noncardiac metastases is essentially similar, except for the greater incidence of skin involvement in the patients with malignant melanoma. Fifty-five (89%) of the 62 patients with splenic metastases had either leukemia or lymphoma; in 11% splenic metastases were due to other tumors.

From the Memorial Center for Cancer and Allied Diseases.

1. (a) Herbut, P. A., and Maisel, A. L.: Secondary Tumors of the Heart, Arch. Path. **34**: 358 (Aug.) 1942. (b) Yater, W. M.: Tumors of the Heart and Pericardium: Pathology, Symptomatology and Report of 9 Cases, Arch. Int. Med. **48**: 627 (Oct.) 1931.
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4. Ritchie, G.: Metastatic Tumors of the Myocardium: A Review of 16 Cases, Am. J. Path. **17**: 483, 1941.
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The sites of cardiac metastases in the 106 cases of leukemia, lymphoma, and visceral and cutaneous tumors were as follows: Pericardial involvement occurred in 27% (29) of the patients, 5.7% (3) of the 52 leukemia patients, 52.9% (9) of the 17 lymphoma cases, and 45.9% (17) of the 37 cases of other tumors. No significant differences were noted in epicardial, myocardial, or endocardial metastases in the three groups, the incidence ranging from 43 to 53%, from 30 to 46%, and from 20 to 27%, respectively. Bloody pericardial fluid was found in 3.8% (2) of the leukemia patients and in 11.7 (2) and 10.8% (4) of the lymphoma and other tumor groups. Gross evidence of tumor invasion of the heart

TABLE 1.—*Incidence of Cardiac Metastases from Visceral and Cutaneous Tumors*

Type	No. of Patients		
	Total	No. with Cardiac Involvement	Percentage
Carcinoma of lung	35	11	31
Carcinoma of breast	27	9	33
Malignant melanoma	5	3	60
Carcinoma of thyroid	15	2	13
Carcinoma of tail of pancreas	4	2	50
Carcinoma of rectum	16	1	6
Carcinoma of stomach	19	1	5
Carcinoma of prostate	5	1	20
Carcinoma of mouth	3	1	33
Carcinoma of kidney	3	1	33
Neuroblastoma	10	1	10
Ewing's tumor	4	1	25
Rhabdomyosarcoma	1	1	100
Renal carcinosarcoma	1	1	100
Medullary fibrosarcoma of bone	1	1	100
Other tumors	155	0	0
Total	304	37	12

TABLE 2.—*Distribution of Metastases in Thirty-Four Patients with Malignant Melanoma*

Site of Metastases *	No. of Patients	Percentage
Heart	15	44
Lymph nodes	28	82
Lung	23	68
Liver	21	62
Skin	19	56
Bone	16	49
Gastrointestinal tract	14	41
Kidney	12	35
Adrenal	12	35
Spleen	10	29
Pancreas	9	26
Genitourinary tract	6	18

* The brain was examined in 29 patients, with metastatic involvement found in 11 cases (38%).

was present in only 9.5% (4) of the leukemia group but was seen in 64.6% (11) of the lymphoma patients and in 72.9% (27) of the other tumor group. Predominant involvement of one chamber of the heart was uncommon in leukemia, with 3.8% (2) encountered in the right atrium, none in the left atrium, 9.5% (5) in the right ventricle, and 7.6% (4) in the left ventricle. In the lymphoma patients the incidence was 17.7% (3), 11.7% (2), 29.5% (5), and 5.9% (1), respectively. In the group of other tumors the right atrium and left ventricle were involved in 35.1 (13) and 40.5% (15), respectively; the right ventricle was the site of metastases in 18.9% (7) and the left auricle in only 8.1% (3). More than one chamber of the heart was involved in 3.8% (2) of leukemia patients, in 23.5% (4) of the lymphoma group, and in 32.4% (12) of the other tumor groups, with an over-all incidence of 16.8% (18 of the 106 patients).

CLINICAL MANIFESTATIONS

The antemortem diagnosis of cardiac metastasis has been made but infrequently,[7] and it seemed worth while to review the clinical data in the 106 patients with proved involvement of the heart by tumor. Fifty-nine patients had electrocardiograms, chest roentgenograms, and adequate clinical data to evaluate the cardiac status. The tumor diagnoses included leukemia in 33, lymphoma 8, bronchiogenic carcinoma 8, adenocarcinoma of breast 3, thyroid carcinoma 2, renal carcinoma 1, medullary fibrosarcoma of femur 1, rhabdomyosarcoma 1, gastric carcinoma 1, and Ewing's tumor 1. Thirty-eight of these 59 patients had no cardiac symptoms or abnormal cardiac physical findings (64.4%). Twelve patients exhibited symptoms and signs that could not be correlated with the presence of cardiac metastases (20.3%). In four instances there was a doubtful relationship between the clinical manifestations and autopsy findings

TABLE 3.—*Distribution of Concomitant Metastases in 106 Patients with Cardiac Metastases*

Site of Metastases	No. of Patients	Percentage
Lymph nodes	103	96
Liver	82	77
Lung	65	61
Kidney	63	59
Spleen	62	58
Bone	50	47
Gastrointestinal tract	35	33
Adrenal	34	32
Pancreas	23	21
Genitourinary tract	19	18
Skin	15	14

(6.8%). In five patients (8.5%) it was reasonable to assume that cardiac symptoms developed as a result of involvement with metastatic disease.

Teleoroentgenograms were even less helpful in arriving at an antemortem diagnosis, since they were within normal limits in 50 instances as far as the heart was concerned. One chest roentgenogram showed the configuration of pericardial effusion, and this effusion was subsequently shown to be due to neoplastic involvement of the pericardium. In two other patients (3.4%) the cardiac silhouette was abnormal, perhaps as a result of the metastases. The abnormalities of the other six teleoroentgenograms (10.2%) could be more logically explained on other bases.

The electrocardiographic tracings of these 59 patients were within normal limits in 25 instances. Of the remaining 34, 9 showed abnormalities probably not related to cardiac metastases. In five such instances there was evidence of electrolyte disturbance associated with the administration of steroids. In others there was electrocardiographic evidence of myocardial and pulmonary infarc-

7. (*a*) De Loach, J. F., and Haynes, J. W.: Secondary Tumors of Heart and Pericardium: Review of the Subject and Report of 137 Cases, A. M. A. Arch. Int. Med. **91**: 224 (Feb.) 1953. (*b*) Dimmette, R. M.: The Antemortem Diagnosis of Secondary Tumors of the Heart: Report of 4 Cases, Armed Forces M. J. **1**: 750, 1950. (*c*) Doane, J. C., and Pressman, R.: Antemortem Diagnosis of Tumors of the Heart, Am. J. M. Sc. **203**: 520, 1942. (*d*) Ritchie.[4] (*e*) Yater.[3b]

tion, subsequently confirmed at autopsy. Eight patients had electrocardiographic changes, the cause of which was obscure, and 17 exhibited abnormalities that were best explained by the metastatic cardiac lesions. From a glance at table 4, it is obvious that the electrocardiographic abnormalities observed were nonspecific and simply indicated the presence of myocardial disease not explainable on any other known basis. T-wave abnormalities were the commonest electrocardiographic evidence of cardiac metastases. The seven patients with low voltage and the five with ST segment deviations had pericardial and/or epicardial involvement at autopsy. It is our impression, both from this study and from the continuing search for evidence of metastases to the heart among the patients treated at Memorial Center, that frequent electrocardiograms will be of considerable value in helping with antemortem diagnosis of this complication.

Table 5 summarizes clinical manifestations noted in the 59 patients and correlates the antemortem status with the degree of cardiac involvement noted at autopsy. No significant differences were noted among the clinical, roentgenographic, and electrocardiographic findings and

TABLE 4.—*Electrocardiographic Findings in Fifty-Nine Patients with Cardiac Metastases*

	No. of Patients	
Normal electrocardiogram	25	42%
Abnormal electrocardiogram	34	58%
	No. of Patients	
Abnormal Electrocardiogram Probably Unrelated to Cardiac Metastases	9	15.2%
Electrolyte imbalance		5
Myocardial infarction, healed		1
Myocardial infarction, acute		1
Pulmonary infarction, acute		1
Right axis deviation		1
Abnormal Electrocardiogram Possibly Due to Cardiac Metastases	8	13.5%
T-wave abnormalities		7
Q-waves		1
Prolonged QT interval		1
Low voltage QRS complexes		1
ST segment abnormality		1
Shifting pacemaker		1
Auricular fibrillation		1
Right bundle branch block		1
Abnormal Electrocardiogram Probably Due to Cardiac Metastases	17	28.8%
T-wave abnormalities		14
Low voltage QRS complexes		7
ST segment deviations		5
Q-waves		2
Prolonged A-V conduction		1
Arrhythmias (1 sinus arrhythmia, 1 auricular fibrillation, and 1 auricular flutter with 2:1 block)		3

the size and degree of cardiac metastases. It is obvious that the number of patients in the various groupings is too small to permit any speculations.

COMMENT

The strong kneading action of heart muscle, its metabolic peculiarities, the restricted lymphatic connections, and the rapid flow of blood through the heart have been advanced as possible explanations of the relatively low incidence of cardiac metastases. Invasion of the heart occurs by embolism in the lymphatic channels or blood vessels or by direct invasion; the frequency is in the order listed even in the case of the more adjacent tumors, such as carcinoma of the lung or breast.[8] Kretz,[9] and others have shown that 75% of the coronary arterial blood flow returns to the right side of the heart via the Thebesian veins and coronary sinus, suggesting that embolic tumor cells may have a greater opportunity to lodge

TABLE 5.—*Relationship of Antemortem Findings to the Degree of Involvement Found at Post Mortem*

Degree of Involvement	No. of Patients	Clinically Abnormal	Roentgenographically Abnormal	Electrocardiographically Abnormal
Slight	10	2	0	3
Leukemia	8	2	0	2
Lymphoma	1	0	0	0
Other tumors	1	0	0	1
Moderate	2	0	0	0
Leukemia	1	0	0	0
Lymphoma	1	0	0	0
Other tumors	0	..	..	..
Marked	6	1	0	2
Leukemia	2	0	0	1
Lymphoma	4	0	0	1
Other tumors	0	..	..	..

in the right chamber of the heart than the left. Our data lend support as far as the right auricle is concerned, but the left and right ventricles were involved with approximately the same frequency.

In our series of 500 autopsies, the heart was invaded by neoplastic disease in 106 instances, or 21%. This relatively high incidence is due, perhaps, in part to the inclusion of a disproportionate number of patients with leukemia or lymphoma, diseases that are associated with a high incidence of cardiac involvement. The fact that 44% of the patients who died of leukemia and 24% of those who succumbed to lymphoma had cardiac involvement is worthy of emphasis, since these diseases are, perhaps, more amenable to treatment by radiation and chemotherapeutic agents. Antemortem diagnosis of cardiac spread of these diseases might permit institution of specific therapy as well as a study of its effects on the heart involvement.

Repeated physical examination may reveal an unexplained tachycardia, a friction rub, or gallop rhythm, which, when taken together with electrocardiographic abnormalities, may permit an antemortem diagnosis of involvement of the heart or pericardium by neoplastic disease. When electrocardiograms are taken at frequent intervals and show definite changes not ascribable to any other form of heart disease, a presumptive diagnosis of metastatic heart disease can be entertained. Unfortunately, the only clue to cardiac involvement in our series of patients was suggested by electrocardiographic means and particularly by changes noted on serial tracings. Tachycardia was noted as frequently in patients without as in those with cardiac metastases. We found no single clinical picture or laboratory finding characteristic of cardiac metastases. It may be of significance that, since this study has started, suspicion of cardiac involvement by neoplastic disease has led in several instances to the premortem diagnosis of cardiac metastases at Memorial

8. Willis, R. A.: The Spread of Tumours in the Human Body, London, J. & A. Churchill, Ltd., 1933, p. 259.

9. Kretz, J.: Über die Bedeutung der Venae minimae Thebesii für die Blutversorgung des Herzmuskels, Virchows Arch. f. path. Anat. **266**: 647, 1928.

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Center for the first time. The diagnosis was suggested by over-all consideration of the patient, together with careful electrocardiographic and roentgenographic studies. Occasionally studies of aspirated pericardial fluid may reveal the presence of cancer cells and help to establish the diagnosis.[7b]

If associated cardiovascular symptoms are also present, consideration of specific therapy in the form of irradiation is in order. Thus far no published data are available regarding the efficacy of such therapy. Moreover, factors such as the stage of the disease, its prognosis, and the sensitivity of the type of tumor to irradiation will limit the number of patients suitable for specific treatment. The frequency of cardiac involvement by leukemic cells or lymphoma, however, justifies continued efforts for early diagnosis of this complication, since these diseases are generally radiosensitive. One patient with Hodgkin's sarcoma showed a return to normal of his electrocardiogram with relief of cardiorespiratory distress following x-ray therapy directed to the heart. This case will be reported in detail separately.

No data are available with regard to the time heart metastases develop in patients with uncontrollable cancer, but the fact that they rarely occur without the presence of widespread metastases is borne out by our studies. No patient had cardiac metastases alone, and in all instances the disease was firmly entrenched in other tissues as well as the heart.

SUMMARY

Cardiac metastases were noted in 21% of 500 consecutive autopsies done on patients who had died of neoplastic disease. Cardiac involvement was found in 44% of the 119 patients who died of leukemia, in 44% of 34 patients with malignant melanoma, in 33% of 27 patients with breast cancer, in 31% of 35 patients with carcinoma of the lung, and in 24% of 69 patients with lymphoma. The pericardium was involved in 5.7% of the leukemia group and was the site of metastases in 49.4% of the remainder. The incidence of epicardial, myocardial, and endocardial metastases varied from 43 to 53%, from 32 to 46%, and from 20 to 27% in the patients who died from leukemia, lymphoma, and the group of other tumors. Gross evidence of tumor involvement was found in 9.5% of the leukemia patients, and in 64.7 and 72.9% of the lymphoma and other tumor groups. Tachycardia was a nonspecific finding, being present in the same frequency in patients who died of cancer without cardiac metastases as the 106 with tumor invasion of the heart. Cardiac metastases were always associated with widespread involvement of many other organs by cancer. Metastatic involvement of the heart was associated with symptoms and physical findings suggestive of heart disease in only 8.5% of the patients. Electrocardiographic findings suggestive but by no means specific were present in 28.8% of the patients with cardiac metastases. The teleoroentgenogram suggested cardiac involvement in 6% of the patients so studied. No correlation was noted between the size and extent of cardiac metastases and the clinical manifestations of heart disease.

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ANTISPASMODIC COMPOUND 08958 IN TREATMENT OF PARALYSIS AGITANS

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The many new drugs introduced in recent years to relieve the tremor, rigidity, and poverty of movement of paralysis agitans (Parkinson's disease) give testimony to the fact that no universally effective treatment for this disorder has been discovered. The introduction of trihexyphenidyl (Artane)[1] was an important advance in therapy, but its effectiveness is limited, and it has not entirely replaced the older solanaceous alkaloids, namely, atropine, scopolamine (Hyoscine), stramonium, and hyoscyamus. Initial successes with synthetic compounds, such as Rabellon,[2] which contains belladonna alkaloids, caramiphen hydrochloride (Panparnit),[3] diethazine (Diparcol),[4] and the antihistaminics, principally diphenhydramine (Benadryl) hydrochloride,[5] were encouraging, but these agents now seem to be inadequate for the majority of patients with paralysis agitans and have, for the most part, been reduced to the status of adjunct drugs. Similarly, agents tending to reduce spasticity, the curare derivatives and mephenesin (Tolserol),[6] seem to have very limited practical value in this disorder.

Perhaps the most significant observation to be made in the clinical study of paralysis agitans is that each patient's care must be strictly individualized. One patient will derive great benefit from a particular drug, while another may find that same substance entirely ineffective. Tolerance to drugs also has great individual variation. These factors emphasize the fact that, until a universally effective symptomatic treatment or cure is found, each patient's therapeutic program must be individually planned. Con-

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Compound 08958 and the chemical and pharmacological information were furnished by the Lilly Research Laboratories, Indianapolis.

Read before the Section on Nervous and Mental Diseases at the 102nd Annual Meeting of the American Medical Association, New York, June 3, 1953.

1. (*a*) Doshay, L. J., and Constable, K.: Artane Therapy for Parkinsonism: Preliminary Study of Results in 117 Cases, J. A. M. A. **140**: 1317 (Aug. 27) 1949; Newer Drugs in Treatment of Parkinsonism, Neurology **1**: 68 (Jan.-Feb.) 1951. (*b*) Corbin, K. B.: Trihexyphenidyl: Evaluation of New Agent in Treatment of Parkinsonism, J. A. M. A. **141**: 377 (Oct. 8) 1949.

2. Vollmer, H.: Comparative Value of Solanaceous Alkaloids in Treatment of Parkinson's Syndrome, Arch. Neurol. & Psychiat. **48**: 72 (July) 1942.

sequently, the greater numbers of preparations available, even though of limited range of therapeutic efficacy, the greater opportunity there is to provide a satisfactory program for each patient. Doshay [1a] recently emphasized this need for newer drugs. It is by virtue of this reasoning that the compound to be described was introduced.[7] This drug is by no means expected to replace any existing medication, but a sufficiently large number of patients have benefited from it to warrant further and more extensive study by different investigators.

CHEMISTRY AND PHARMACOLOGY

Compound 08958 is an aminopropanol with the chemical formula of 1-phenyl-1-cyclopentyl-3-piperidino-1-propanol hydrochloride. It, therefore, bears resemblance to trihexyphenidyl, the latter being 1-hydroxy-1-phenyl-1-cyclohexyl-3-piperidinopropane hydrochloride. The chemical structure is illustrated in the figure. Compound 08958 is supplied as the hydrochloride salt. It is a white crystalline solid and is extremely bitter to the taste.

Compound 08958 exhibits an activity approximately equal to that of atropine on isolated guinea pig intestinal strips stimulated with mecholyl or acetylcholine. On similar test preparations, it showed practically no antihistamine activity. In similar tests in which isolated strips of uterine muscle from the guinea pig were employed, Compound 08958 showed no effect. In trained dogs with Thiry fistulas, spasmolytic action on small intestines was about one-half that procurable with atropine when both agents were given intravenously. Effectiveness of Compound 08958 by oral administration could be demonstrated in anesthetized cats.

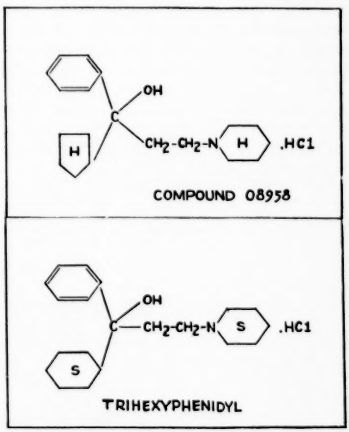
When Compound 08958 was administered intravenously in large doses to dogs, a fall in blood pressure with fairly slow recovery was observed. The manifestation was less acute with smaller doses. Respiratory stimulation followed the fall in blood pressure and was believed to be a secondary phenomenon to the hypotension.

Compound 08958 was about one-tenth as effective as atropine in blocking salivary flow in anesthetized dogs. Similarly, in anesthetized cats the drug was one-tenth as effective as atropine in blocking cardioinhibitory fibers of the vagus nerve. Mydriatic and slight local anesthetic activity could be demonstrated when solutions prepared from Compound 08958 were placed in the conjunctival sacs of albino rabbits.

Toxicity studies in rats and mice disclose Compound 08958 to be slightly, but not markedly, more toxic than atropine by either oral or intravenous administration. Chronic toxicity tests in rats over a one month period showed no evidence of damage, either grossly or microscopically.

PROCEDURE

A total of 67 patients were treated on the neurology service of the University Hospital. No selection was made as to type or severity of the paralysis agitans; each patient was accepted as he or she appeared at the clinic. It is known that it is extremely difficult to evaluate objectively the results of treatment in paralysis agitans. Even refined methods of testing fail to be conclusive in a disorder in which the patient's condition changes from moment to moment depending on his emotional reaction to coming to the clinic, the reaction to the physician and the examination, the state of fatigue, and the general physical condition. Even placebo controls mean very little when it is remembered that a patient who receives good relief from a new medication might well fail to report lack of benefit when placed on placebos, thereby admitting to himself that the new agent he had found and in which he had developed hope and faith was, in reality, worthless. In an attempt to diminish the suggestive connotations of treatment with a new drug, each patient was told that he or she was to be given a trial on several new drugs, any or all of which might help or prove worthless. In this way the patient was able to choose which of the new drugs, if any, he preferred without having to place all his faith in any one drug; he could, therefore, more realistically evaluate each medication.



For comparison the structural formulas of Compound 08958 and trihexyphenidyl (Artane) are illustrated.

To be considered useful, certain qualifications had to be fulfilled by the experimental drug: (1) it should give some degree of subjective relief to the patient's symptoms; (2) it should produce some objective evidence of improvement on neurological examination; (3) it should be as effective as the drugs already available or, if not as effective, should have some use as an adjunct

3. Dunham, W. F., and Edwards, C. H.: Parkinsonism Treated with Panparnit, Lancet **2**: 724 (Nov. 6) 1948. Schwab, R. S., and Leigh, D.: Panparnit in Treatment of Parkinson's Disease, J. A. M. A. **139**: 629 (March 5) 1949.

4. Palmer, H., and Black, H.: Diparcol Therapy for Parkinsonism, New Zealand M. J. **48**: 487 (Oct.) 1949.

5. McGavack, T. H.; Elias, H., and Boyd, L. J.: Some Pharmacological and Clinical Experiences with Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl), Am. J. M. Sc. **213**: 418 (April) 1947. Budnitz, J.: Use of Benadryl in Parkinson's Disease: Preliminary Report of 8 Cases, New England J. Med. **238**: 874 (June 17) 1948.

6. Stephen, C. R., and Chandy, J.: Clinical and Experimental Studies with Myanesin (Preliminary Report), Canad. M. A. J. **57**: 463 (Nov.) 1947. Schlesinger, E. B.; Drew, A. L., and Wood, B.: Clinical Studies in Use of Myanesin, Am. J. Med. **4**: 365 (March) 1948. Berger, F. M., and Schwartz, R. P.: Oral "Myanesin" in Treatment of Spastic and Hyperkinetic Disorders, J. A. M. A. **137**: 772 (June 26) 1948.

7. Magee, K. R., and DeJong, R. N.: Treatment of Parkinsonism with New Antispasmodic Compound: A Preliminary Report, Univ. Michigan M. Bull. **19**: 59 (March) 1953.

drug; and (4) the toxicity of the drug should not outweigh the beneficial effects.

The patients were thoroughly questioned regarding both their over-all impressions on the effect of the drugs and the presence of side-effects. For more critical appraisal they were asked to observe and report changes in specific daily activities, such as the alteration in the tremor while eating, dressing, shaving, or working, and to record alterations in gait, articulation, strength, and rigidity. Frequent examinations were carried out to observe changes in the tremor as brought out by improvement in holding objects, dressing, and writing. Changes in rigidity, associated movements, strength, speech, posture, and ability to perform skilled movements with greater ease and speed were similarly evaluated.

The majority of patients had taken either scopolamine or trihexyphenidyl, or both, and the effectiveness of these compounds and other drugs was noted and compared. Several other experimental drugs were used either before or after treatment with Compound 08958. If the patient reported best results with Compound 08958 after failure with the other experimental preparations, he again received it for prolonged trial.

RESULTS

The results of therapy with Compound 08958 are illustrated in table 1. Patients were divided into four groups. Group A consisted of those in whom Compound 08958 gave relief superior to that obtained by previous standard medications, trihexyphenidyl or scopolamine in the great majority, and also produced definite objective evidence of improvement on neurological examination, but did not cause significant side-effects when given in adequate therapeutic doses. Group B included those patients who found no difference between Compound 08958 and the previous medications. Objective evidence of improvement above that obtained with no treatment was essential. In group C were those patients who received some benefit from Compound 08958, but not as much as with previous medications. Patients in whom Compound 08958 was either ineffective or produced side-effects serious enough to preclude its use were placed in group D.

TABLE 1.—*Results of Therapy with Compound 08958*

Type of Paralysis Agitans	No. of Patients	Group A		Group B		Group C		Group D	
		No.	%	No.	%	No.	%	No.	%
Idiopathic	31	16	52	8	26	2	6	5	16
Postencephalitic	20	11	55	5	25	4	20	0	0
Arteriosclerotic	10	1	10	2	20	4	40	3	30
Totals	61	28	46	15	25	10	16	8	13

Of 61 patients with paralysis agitans, a total of 28, or 46%, found relief with Compound 08958 superior to that obtained with any other medication, while 15, or 25%, found no difference between the benefit of this compound and previous drugs. It was noted that patients with either idiopathic or postencephalitic disease made up the larger percentage of those in the first group (relief superior to that with other medications), the actual figures being 52 and 55%, respectively.

Table 2 shows the relative improvement in each component of the disease, using the same groups for classification as in table 1. As is true with the other atropine derivatives, rigidity was helped the most, but an unusually large number of patients felt that their tremor was materially improved.

Of particular interest are the four patients who received remarkable relief from oculogyric crises. Three of these patients have taken Compound 08958 for more than nine months with dramatic decrease in the frequency of the oculogyric attacks, but with abrupt recurrence if they stop taking the drug for several days. The fourth patient received complete relief from the attacks, but found Compound 08958 (and also its placebo preparation) so toxic that it had to be discontinued.

TABLE 2.—*Improvement in Major Symptoms After Therapy with Compound 08958*

Symptoms	Group A		Group B		Group C		Group D	
	No.	%	No.	%	No.	%	No.	%
Tremor	29	58	14	28	5	10	2	4
Rigidity	30	64	12	26	3	6	2	4
Bradykinesis	27	69	11	24	3	7	4	9
Oculogyria	4	100	..	..	..	..	..	..
Blepharospasm	..	..	1	50	..	..	1	50

Six patients in the series did not have paralysis agitans. Of these, only one patient with dystonic movements of his upper extremities obtained good results with Compound 08958. The other diagnoses were familial tremor, senile tremor, congenital athetosis, spastic pseudosclerosis, and the Hallevorden-Spatz syndrome. These patients received no benefit from Compound 08958 and experienced toxic reactions on relatively small doses.

Compound 08958 was available in 2.5 and 5 mg. tablets. Attempts were made to standardize dosage. It was evident that there was an extremely wide variation in the optimum therapeutic dose. The best results were obtained in the postencephalitic group, as is usually true when using atropine derivatives. This may well be due to the fact that these patients could tolerate much larger amounts of medication. Several patients were maintained on 30 to 50 mg. of Compound 08958 each day without apparent adverse effect. On the other hand, those with idiopathic and arteriosclerotic conditions could not tolerate the medication nearly as well. It became evident that, to secure maximum beneficial results, it was best to begin each patient on a very small dose, such as 2.5 mg. once each day, and to increase the dose by one tablet every two or three days to the point of tolerance. To patients giving a strong history of intolerance to the atropine derivatives, one-half of the 2.5 mg. tablet was given once daily; this amount was increased slowly as it was established that the patient could tolerate the preceding day's dose.

Significant side-effects consisted of dry mouth, dizziness or light headedness, blurred vision, nausea, weakness, and epigastric discomfort. In addition, the most serious side-effects of confusion and disorientation occurred early in the study when, after the initial high tolerance of the first few patients, each patient received 5 mg. tablets of Compound 08958 three times daily as a starting dose. The side-effects cleared promptly when the medication was discontinued or the dose was reduced.

Several patients who experienced severe reactions on the 5 mg. tablets are classified as poor results, although

those who were again placed on Compound 08958 in smaller doses often experienced very good results. Two patients classified as poor results because of severe reactions noted the same side-effects when they were given a placebo preparation of Compound 08958. The number and percentage of side-effects are listed in table 3.

TABLE 3.—*Side-Effects in Patients Receiving Compound 08958*

Type	No. of Patients	%
Dry mouth	22	36
Blurred vision	7	11
Dizziness	15	25
Palpitation	2	3
Epigastric discomfort	5	8
Nervousness	7	11
Insomnia	1	2
Salty taste	3	5
Weakness	2	3
Nausea	3	5
Numbness	3	5
Disorientation	2	3

From this series, it is evident that a given dose of Compound 08958 is considerably more potent than trihexyphenidyl in both beneficial effect and side reactions. Twenty-one patients were known to have previously taken scopolamine, and, of these, 17 preferred Compound 08958. Forty patients were known to have taken trihexyphenidyl, and, of these, 21 preferred Compound 08958, 7 preferred trihexyphenidyl, and 12 could see no significant difference.

COMMENT

Many drugs have been introduced in the treatment of paralysis agitans with early enthusiasm only to be proved later to be of little or no value. This leads us to interpret the results obtained in this series cautiously and to keep in mind the many variables in evaluation as outlined above. Of course, final conclusions will depend on larger groups of statistics by different investigators. It does, however, seem safe to conclude that preliminary studies have demonstrated that Compound 08958 has been of value in a limited series of patients with paralysis agitans and that it should be studied further to ascertain its definitive place in the physician's armamentarium for the treatment of this disorder.

SUMMARY

A series of patients with paralysis agitans (Parkinson's disease) received a therapeutic trial with the antispasmodic, Compound 08958 (1-phenyl-1-cyclopentyl-3-piperidino-1-propanol hydrochloride). Of these patients, 46% received beneficial results superior to those obtained by standard medications. Side-effects were similar to those produced by other atropine derivatives. Careful adjustment of dosage was necessary to minimize these side reactions.

ADDENDUM

Since this article was prepared, Compound 08958 has been released by the Eli Lilly Company under the trade name Pagitane hydrochloride in 1.25 and 2.5 mg. tablets.

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BLOOD AND SPINAL FLUID TESTS FOR REAGIN AFTER TREATMENT OF NEUROSYPHILIS

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It has long been known that in patients treated for late neurosyphilis blood serum and spinal fluid tests for syphilis continue to give positive results for varying periods after treatment. Yet, many patients are still treated unnecessarily in the hope of reversing such positive reactions. This practice continues because few reports on the long-term follow-up of large series of patients have been published. Physicians are disturbed by the great variety of serologic responses that may be encountered in treated patients, some of whom become seronegative relatively soon while others remain seropositive for years. Even more disconcerting are the great fluctuations in titers obtained in quantitative tests and the great discrepancies in titers obtained by different kinds of tests that occur in some patients and not in others. Such serologic phenomena are not easily interpreted, but, as this report attempts to show, the persistence of reagin in varying amounts following treatment of known syphilis does not necessarily indicate the persistence of an active infection.

At Bellevue Hospital, 396 patients have been followed for more than five years after treatment of neurosyphilis with either malaria or penicillin. Neurosyphilis was chosen for the presentation of follow-up data because there was no question about the diagnosis of syphilis in patients with this complication. When first treated at Bellevue Hospital, all patients had active neurosyphilis, as shown by spinal fluid examinations. In my judgment, the neurosyphilis has been permanently inactivated in all of these patients for more than five years, despite numerous vagaries in the titers obtained in serologic tests for syphilis.

The concept of differentiating between activity and inactivity of neurosyphilis by means of spinal fluid examinations has been described by Dattner and me in numerous papers.[1] Briefly, we have shown that active neurosyphilis is best demonstrated by pleocytosis in association with positive results in specific tests of the spinal fluid for syphilis. After successful treatment, the spinal fluid cell count should become normal within three to four months and should remain normal, and there should be a more gradual improvement of results in other quantita-

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From the New York State Department of Health, the Department of Medicine, New York University-Bellevue Medical Center, and the Service of Syphilology, Bellevue Hospital.

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tive tests of the spinal fluid. The persistence of reagin in the spinal fluid for years after treatment does not prove that the disease is active, but high reagin titers usually show a significant decline during the first year after successful treatment. The clinical manifestations of neurosyphilis are, of course, important, but, obviously, normal function of permanently damaged tissues in the central nervous system cannot be restored by the killing of spirochetes. Clinical manifestations are indications of active disease only when there is unquestioned evidence of progressive disease.

This report is not to be construed as an evaluation of the relative effectiveness of malaria and penicillin therapy. Its purpose is rather to show what can be expected from tests for reagin performed after syphilis has been arrested by treatment, as shown by spinal fluid and physical examinations. No patients in this series showed clinical evidence of progressive neurosyphilis after the last treatment.

METHOD

The period of follow-up for each patient dates from the completion of the last successful treatment, as previously defined. Over 50% of patients in both groups prior to malaria or penicillin therapy had received varying amounts of metal therapy, sometimes irregularly for years, without permanent arrest of the infection. Serologic tests for syphilis were performed, as a rule, every two or three months during the first year after treatment and at three to six month periods thereafter. Spinal fluid examinations were made in most cases three to four months after treatment and at six month intervals thereafter. The latter schedule could not be completed for all patients, but, with few exceptions, every patient had at least one spinal fluid examination each year until two completely normal reports were received, and in numerous patients the examinations were continued yearly after results of all spinal fluid tests had become normal.

Several patients in each group who had no evidence of clinical relapse or of pleocytosis were retreated for the sole purpose of noting the effect on persistently high blood serum reagin titers. In these cases, the follow-up dates from the time the patients received therapy resulting in normal cell counts and decreases in spinal fluid reagin titers. Retreatment in such case had no significant effect on the titers of either the blood serum or the spinal fluid. Not only in patients with neurosyphilis but also in those with other forms of late syphilis I have proved to my satisfaction the futility of prolonging treatment or of retreatment for the sole purpose of lowering high reagin titers.

FOLLOW-UP OF MALARIA-TREATED PATIENTS

Patients treated with malaria received 10 daily injections of 0.06 gm. of oxophenarsine hydrochloride following the last fever and no subsequent therapy except for reasons previously outlined. The malaria-treated group consisted of 183 patients who were followed for 5 to 14 years after the last treatment. Two tabetic patients in the series had negative blood serologic test reactions when treated with malaria but they had active neurosyphilis, as indicated by spinal fluid examinations. They are excluded from table 1, which gives data on the persistence of positive serologic test reactions following treatment. One patient who was followed for more than six years with serologic tests had no spinal fluid examination after the first four years after treatment. This patient is included in table 1 but excluded from table 3, which gives data on the spinal fluid tests. The entire group is classified by race and sex: white males, 122; white females, 34; Negro males, 19; Negro females, 6; and Chinese males, 2.

Serologic Test Data.—The blood serum examinations in the early years of follow-up were done with qualitative Kahn and Wassermann tests at the Bellevue Hospital laboratory. From 1943, quantitative Kahn tests were done in the New York University-Bellevue Medical Center laboratory, and quantitative complement fixation tests were done by the New York State Department of Health laboratory. Additional Kolmer complement fixation tests were done in some cases. No patient was counted as having negative test results unless the results from all types of tests used were completely negative. During a follow-up of several years' duration, negative results from one or more serologic tests are frequently interspersed between slightly positive test results, and occasionally the titers in one or more tests fluctuate greatly. Minor variations in titers are probably caused by varying sensitivity of the tests, but extreme fluctuations may be due to intercurrent infections or unknown causes. In either case, a reactivation of syphilis cannot be assumed to have occurred when positive serologic test results are reported subsequent to negative tests results or when, in the case of positive results, the titers fluctuate, unless significant increases in titers from previous levels persist for several months.

Our present ignorance of the true nature of serologic tests for syphilis is emphasized not only by fluctuations in titers but also by the frequently occurring discrepancies among titers from different tests performed on the same specimen of blood. In my experience, wide fluctuations in titers may be reported for one test but not for another, or there may be for years pronounced sustained discrepancies in the titers obtained by different tests. The occurrence of such discrepancies suggests that the reagin tested for in the blood serum is a complex substance that may consist of more than one presumed antibody or that in some persons inhibitory substances interfere with the demonstration of reagin more in some tests than in others. The wide fluctuations in titer following treatment suggest that factors other than syphilis influence the tests in known syphilitic patients as well as in persons who have biologically false positive reactions to tests for syphilis. Whatever the explanation may be for the bizarre serologic patterns noted in a prolonged follow-up of treated syphilitic patients, it is reasonably certain that, in the absence of other evidences of relapse or progression of the disease, they do not indicate continued activity of the syphilitic process, and treatment should not be continued solely on the basis of such serologic patterns.

When the patients were last examined, the titers in all except a few serologic tests recorded as positive were relatively low (positive in dilutions of 1:2 or less or in units of less than 10), but positive test results with high dilutions on at least one occasion persisted for more than two years in a number of patients, who were retreated for that reason. As previously noted, retreatment did not result in lower titers.

Table 1 shows the number of patients followed for various periods (years) after treatment was stopped, the numbers still seropositive at the designated intervals, and the number becoming seronegative each year after cessation of treatment. To obtain the total number of patients who became seronegative, the numbers becoming negative each year must be added.

To obtain a possibly more accurate estimate of prolonged seropositivity, modified life table methods were used to compute the percentage expected to be seropositive for each designated period after the sixth year of follow-up. The results are shown in table 2. Because of the relatively small number followed for more than 11 years, estimated percentages by life table methods after the 10 to 11 year period are not given. Of the patients actually followed for 10 to 11 years, 71.7% were still seropositive (table 1) as compared to an estimated 62.8% who would be seropositive if all patients had been observed for that period (table 2).

TABLE 1.—*Results of Follow-Up Serologic Tests for Syphilis in Malaria-Treated Neurosyphilitic Patients with No Evidence of Clinical Relapse or Progression of Disease*

	Yr. After Treatment												
	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	12-13	13-14
No. followed	181	181	181	181	181	169	154	137	119	92	55	24	7
No. still positive	173	166	166	159	152	140	126	109	93	66	35	15	5
% still positive	95.6	91.7	91.7	87.8	84.0	82.7	81.8	79.6	78.2	71.7	63.6	62.5	71.4
No. becoming negative each yr.	8	7	0	7	7	5	4	5	5	9	3	0	1

TABLE 3.—*Results of Follow-Up Tests for Spinal Fluid Reagin in Malaria-Treated Neurosyphilitic Patients with No Evidence of Clinical Relapse or Progression of Disease*

	Years After Treatment												
	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	12-13	13-14
No. followed	182	182	182	182	182	170	155	139	121	94	56	25	7
No. still positive	162	155	141	132	116	92	77	62	45	26	10	4	1
% still positive	89.0	85.2	77.5	72.5	63.7	54.1	49.7	44.6	37.2	27.7	17.9	16.0	14.3
No. becoming negative each yr.	20	7	14	9	16	17	6	7	7	2	2	0	0

Spinal Fluid Test Data.—Spinal fluid specimens from patients treated with malaria were examined by means of the Bellevue Hospital Wassermann test during the early years of the study but subsequently were tested with the quantitative complement fixation test for syphilis that is used in the New York State Department of Health laboratory. Results of the latter test are reported in units. In my experience, it is an exceptionally reliable test but is less sensitive than the Kolmer complement fixation test. After 1948, the Kolmer test was used in addition to the New York State test for all patients in the penicillin-treated group but not for all in the malaria-treated group.

Table 3 shows the results of spinal fluid test follow-up in the same manner as results of serologic tests are shown in table 1. The bizarre serologic patterns noted in the blood serum of some patients were not found in the spinal fluid. Consequently, the reagin present in spinal fluid seems to be less influenced by unknown factors than is the reagin in blood serum. When spinal fluid reagin was found in a relatively large amount at the time of treatment, the titer invariably fell significantly within six months to a year after treatment, but it frequently remained at low levels for years without evidence of clinical progression. Patients with low spinal fluid reagin titers, when treated, often continued to have low titers for varying periods after treatment. When last examined, only six of the malaria-treated patients had spinal fluid reagin titers of more than 10 units. In general, reagin disappears more rapidly from the spinal fluid than from the blood serum, but the reverse may be true. As shown in table 3, more patients had negative results in tests for reagin in the spinal fluid than in tests for reagin in the blood serum, but the percentage of those who continued to have slightly positive spinal fluid test results for 10 years or more is higher than I anticipated.

Persistence of demonstrable reagin in the spinal fluid does not necessarily prove persistence of the syphilitic infection in the central nervous system, and it certainly does not prove failure to arrest the infectious process. My experience shows that if the spinal fluid cell count has become normal and there has been improvement in results of other spinal fluid tests for two years after treatment, the infection may be confidently expected to have been permanently arrested. At Bellevue Hospital, I have never observed relapse of neurosyphilis, as shown by an increased cell count and increases in results of other quantitative tests of the spinal fluid, more than two years after treatment, even though demonstrable reagin was still present.

Table 4 shows the types of neurosyphilis for which malaria treatment was given and gives the percentage of patients in each classification who had negative spinal fluid test results when last examined. The high percentage of negative results found in the asymptomatic group is probably best explained by the fact that most of the patients in this class were relatively young and presumably had had syphilis for a shorter time than most of the patients in other classifications; however, no patient in whom the duration of syphilis was known to be less than two years is included in this report. Age is not a determining factor in the duration of positive results in tests for spinal fluid reagin after treatment, but the duration of the infection usually is, even though occasionally

patients treated for syphilis of only two years duration may have positive blood and spinal fluid test results for years after treatment.

FOLLOW-UP OF PENICILLIN-TREATED PATIENTS

For comparison with the malaria-treated series, only penicillin-treated patients who have been followed five years or more are included in this report. The penicillin dose varied from 2 to 9 million units, except in a few cases in which it was much higher because retreatment was necessary for relapse. Most of the patients received either 6 or 9 million units. Penicillin was not used to treat neurosyphilis at Bellevue Hospital until April, 1944, and treatment was started with doses that proved too low. The series followed for five years or longer consists of 213 patients. It was composed of 109 white males, 32 white females, 38 Negro males, 21 Negro females, and 10 males and 3 females who were Puerto Rican or Chinese.

TABLE 2.—*Percentage of Patients with Blood Serum and Spinal Fluid Positive for Reagin at Stated Intervals After Treatment of Neurosyphilis, Estimated by Modified Life Table Analysis*

Yr. After Treatment	% of Patients with Positive Serologic Test Results		% of Patients with Positive Spinal Fluid Test Results	
	Malaria-Treated	Penicillin-Treated	Malaria-Treated	Penicillin-Treated
6-7	81.1	72.6	53.8	62.7
7-8	78.6	66.2	49.9	61.1
8-9	75.2	....	44.8	....
9-10	71.4	....	38.8	....
10-11	62.8	....	36.0	....

Serologic Test Data.—Because all the penicillin-treated patients were studied with quantitative complement fixation and Kahn tests from the beginning of treatment, it is possible to give more accurate data on discrepancies in the titers obtained by different serologic tests and on fluctuations of titer than was the case with the malaria-treated group. At the time of treatment with penicillin, 24% had titers of 20 or less; 41% had titers between 20 and 60: and 35% had titers of 60 or higher.

TABLE 4.—*Diagnostic Classification of Malaria-Treated Patients and Percentage with Normal Spinal Fluid When Last Examined*

Diagnosis	No. of Patients	Patients with Normal Spinal Fluid When Last Examined	
		No.	%
Asymptomatic neurosyphilis	20	16	80.0
Meningovascular syphilis	54	35	64.8
Tabes dorsalis	57	33	57.9
General paresis	29	14	48.3
Taboparesis	22	9	40.9
Total	182	107	58.8

That there may be pronounced discrepancies in the results from various serologic tests in cases of active neurosyphilis is shown by the facts that, when treated with penicillin, eight patients had negative results with the Kahn test and positive results with the complement fixation test, two had positive Kahn test results and negative complement fixation test results; nine had low titers in the Kahn test and high titers in the complement fixation test (i. e., Kahn test titers of 4 or less and complement fixation test titers of 32 or higher), and 1 had a titer of 64 in the Kahn test and extremely low titers in the complement fixation test.

Following treatment, pronounced fluctuations in the titers of one or more tests occurred in 20 (9%). These results included such findings as a positive serologic test result of 4 or more units interspersed between negative test results or pronounced increases in titer with subsequent drops, e. g., increases from 4 to 64 units followed by rapid or gradual falls to previous levels. When last examined, 75 patients (35%) showed marked discrepancies in titers determined in various serologic tests, 33 had negative Kahn and positive complement fixation test results, and 2 had positive Kahn and negative complement fixation test results. The greatest discrepancies occurred between the Kolmer complement fixation test and the Kahn test. As performed at the New York University-Bellevue Medical Center, the Kolmer test was usually the most sensitive of the three, and usually its results were reported in higher units than those of the New York State complement fixation test. Examples of extreme discrepancies are those in the cases of three patients in whom the Kahn test results became negative after treatment and remained negative throughout the subsequent years of follow-up while the Kolmer test titers were never lower than 64 units. Four patients had negative Kahn test results and positive Kolmer test titers of 32 when last examined, and two had Kahn test titers of 64 and complement fixation test titers of less than 10.

TABLE 5.—*Results of Follow-Up Serologic Tests for Syphilis in Penicillin-Treated Neurosyphilitic Patients with No Clinical Evidence of Relapse or Progression of Disease*

Yr. after treatment	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9
No. followed	213	213	213	213	213	131	77	19
No. still positive	201	194	186	181	171	95	51	12
% still positive	94.4	91.1	87.3	85.0	80.3	72.5	66.2	63.2
No. becoming negative each yr.	12	7	8	5	10	10	5	0

As previously mentioned, findings such as these emphasize our present ignorance of the composition and formation of reagin in the blood serum, where its presence in some syphilitic, as in some nonsyphilitic persons, apparently is influenced by factors other than syphilis, since I had no reason to believe from clinical and spinal fluid examinations that syphilis was active in any patient. As a matter of fact, all tests for reagin are based on the principle of identifying antibodies, and, by analogy with other antibodies, it is not surprising that reagin should continue to be found in blood serum and spinal fluid long after the syphilitic infection has been arrested or cured. Also, in view of the tendency of some persons to have reagin in the blood serum (but not in the spinal fluid) from causes other than syphilis, the fluctuations in serologic test titers after treatment might have been anticipated.

In table 5 data on the serologic tests done in the penicillin-treated patients are summarized. Comparison of table 5 with table 1 shows that higher percentages of malaria-treated patients than of penicillin-treated patients remained seropositive for longer periods. This finding cannot be interpreted as necessarily implying that

penicillin was a more effective treatment than malaria, since, as previously noted, persistence of reagin after treatment does not prove continued activity of the infection.

Spinal Fluid Test Data.—Only 203 patients are included in the report on spinal fluid tests in table 6, because 10 patients who were followed with serologic tests for more than five years refused to have spinal fluid examinations after the third or fourth year. Table 6 shows that, for the 5 to 6 year period of follow-up, the percentage of patients with positive spinal fluid test results is almost exactly the same as in the malaria-treated group. After the sixth year, however, lower percentages are found in the malaria-treated group. The pronounced drop in penicillin-treated patients followed after the sixth year may have influenced the percentages after the 5 to 6 year period of follow-up, but a much better explanation is available. Ten patients recorded as having positive spinal fluid test results in table 6 had negative New York State complement fixation test results and slightly positive Kolmer test results when last examined and, thus, by definition were classified as having spinal fluid positive for reagin. The Kolmer test was not done on many of the malaria-treated patients. In table 7 the various types of neurosyphilis are classified, and the percentage of patients in each classification who had completely negative spinal fluid test results is shown.

TABLE 6.—*Results of Follow-up Tests for Spinal Fluid Reagin in Penicillin-Treated Neurosyphilitic Patients with No Evidence of Clinical Relapse or Progression of Disease*

Yr. after treatment	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9
No. followed	203	203	203	203	203	125	76	19
No. still positive	187	172	155	142	129	69	40	10
% still positive	92.1	84.7	76.4	69.9	63.5	55.2	52.6	52.6
No. becoming negative each yr.	16	15	17	13	13*	1*	1*	0*

* In comparing these data with those in table 3 it should be noted that three additional patients in the 5-6 year period, two each in the 6-7 and 7-8 year periods, and three in the 8-9 year period had negative results in the New York State complement-fixation tests of the spinal fluid but positive results in the Kolmer tests. The latter tests were not done on most of the malaria-treated group.

TABLE 7.—*Diagnostic Classification of Penicillin-Treated Patients and Percent with Normal Spinal Fluid When Last Examined*

Diagnosis	No. of Patients	Patients with Normal Spinal Fluid When Last Examined	
		No.	%
Asymptomatic neurosyphilis	40	27	67.5
Meningovascular syphilis	48	20	41.7
Tabes dorsalis	53	16	30.2
General paresis	41	7	17.1
Taboparesis	18	6	33.3
Spastic paraplegia	3	0	00.0
Total	203	76	37.4

Table 2 gives the estimates obtained by modified life table methods, of the probable percentages of patients who would have been found to have positive serologic test results and positive spinal fluid test results if all patients had been observed for the specified periods. When the previously mentioned variables are considered, the differences in the percentages between the malaria-treated and penicillin-treated groups are not significant. Even if they were, they could not be used to evaluate the effectiveness of treatment for the reasons mentioned.

SUMMARY

1. From data obtained in a 5 to 14 year follow-up of 181 patients treated for neurosyphilis with malaria therapy and a 5 to 8½ year follow-up of 213 similar patients treated with penicillin, it was found that positive results from serologic tests for syphilis persisted in 80 to 84% of patients followed for 5 years and in 70% of patients followed for 10 years after treatment. 2. Positive results from tests for spinal fluid reagin were found in 63% of patients followed for 5 years and in 27.7% of patients followed for 10 years after treatment. 3. The futility of retreating patients solely because of the persistence of reagin in blood serum and spinal fluid is stressed. In cases in which retreatment was given to note the effect on high titers of blood or spinal fluid reagin no appreciable change in titers was obtained. 4. During the years of follow-up, pronounced discrepancies among the titers obtained by different types of serologic tests occurred in many patients in both groups (in 35% of those treated with penicillin). Fluctuations in the titers obtained with a single type of test occurred with one or more of the serologic tests in some patients in both groups (in 9% of those treated with penicillin). 5. It is suggested that reagin in the blood serum is a complex substance consisting of more than one presumed antibody and that factors other than syphilis may influence the production of one or more of these "antibodies" in known syphilitic patients as well as in persons who have biologically false positive results in tests for syphilis. 6. Spinal fluid reagin is rarely influenced by the unknown factors that affect blood serum reagin and cause changes in serologic test results. 7. Relapse of neurosyphilis, as determined by increases in spinal fluid cell count and in results of other quantitative spinal fluid tests, never occurred later than two years after treatment had inactivated the infection.

39 Columbia St. (7).

Human Engineering.—Until quite recently it was accepted that the equipment a human operator had to use was fixed by engineering considerations only and was not thereafter open to change. Efforts to secure better man-machine performance were made by selecting operators with especially good aptitude or by giving them extensive training on the task. This is a rather wasteful procedure, because a proportion of potential operators must be rejected, because the selection process and training have to be kept going, and because, in spite of all this, the overall results may be below expectation. . . . During the second World War the need for getting efficient performance out of communication and control systems containing human operators brought into being a field of study known variously as ergonomics, biotechnology and work space design, but perhaps best as "human engineering." Human engineering is a blend of various biological sciences—physiology, anatomy, physical anthropology and especially applied experimental psychology, together with various branches of engineering. It aims to determine human capacities, to provide principles governing the design of machines for efficient human use, and to ensure an effective integration of man and machines for the accomplishment of an overall task.—J. C. Lane, M.D., Human Engineering: A New Technology, *Medical Journal of Australia*, July 4, 1953.

CLINICAL NOTES

CHLORDANE INTOXICATION

REPORT OF A CASE

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and
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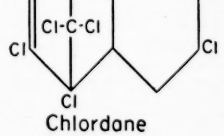
Chlordane is a recently developed insecticide with the empiric formula $C_{10}H_6Cl_8$. This chlorinated hydrocarbon is said to be 1,2,4,5,6,7,8,8-octachloro 2,3,3a, 4,7,7a-hexahydro 4,7-methanoindene, with the structural formula shown in figure 1.

The commercially available technical product is not a pure substance, but contains in addition to chlordane some five or six closely related compounds whose respective proportions may vary.[1] The formulations of technical chlordane include oil solutions, emulsions, dusts, and wettable powders. These find extensive use in the eradication of such household pests as flies, cockroaches, fleas, and mosquitoes as well as agricultural crop enemies such as grasshoppers and certain beetles. Because of the widespread domestic, industrial, and agricultural distribution of the various preparations of chlordane, cases of accidental poisoning may be expected from time to time. These should be reported in order to alert physicians to the early recognition and proper treatment of chlordane intoxication.

The toxic action of chlordane on laboratory animals has been rather extensively studied. Stohlman, Thorp, and Smith [2] determined the LD_{50} of chlordane administered orally as a single dose in olive oil to be in the range of 200 to 250 mg. per kilogram of body weight for rats and 300 mg. per kilogram for rabbits. The rats given fatal doses usually exhibited dyspnea, labored respirations, tremors, convulsions, and coma before death, and the changes in these animals most frequently noted post mortem were ileitis, mottled liver, and pulmonary congestion, which was usually associated with focal hemorrhages. Stohlman and Smith [3] found that rabbits acutely poisoned with chlordane exhibited generalized tremors, opisthotonos, and tonic and clonic convulsions, and that these changes were diminished or abolished by appropriate doses of barbiturates. The LD_{50} of chlordane administered intravenously was increased in amounts approximating 20 to 60 mg. per kilogram in rabbits treated with these drugs.

In chronic toxicity studies reported by Stohlman and his associates,[2] rats that were given a semisynthetic diet containing 0.1% of chlordane usually died in about 10 days, and impaired liver function was demonstrated in rats that were similarly given smaller doses. The principal necropsy findings in rabbits in which chronic intoxication was produced through inclusion of chlordane in the diet were fatty and hyaline degeneration of the liver cells, degenerative changes in the proximal convoluted renal tubules, a low grade enteritis, and exudates throughout the pulmonary passages and alveoli. Albuminuria was a common development in nearly all of such rabbits. Lehman [4] found that dogs are more susceptible to chronic poisoning by chlordane than are rats. Ingle and others [5] have expressed the belief that chlordane is stored in the body in adipose tissue. Ingle reported that a group of rats that had been maintained for 80 weeks at dietary levels of 150 ppm of chlordane did not exhibit the hyperexcitability and tremors that are considered to be the earliest manifestations of chlordane intoxication in rats. When food was withheld from four of these rats, they all died after 36 hours, exhibiting the changes characteristic of poisoning by chlordane. The inference was drawn that lethal doses were released from storage when fats were mobilized in response to starvation.



Chlordane

Fig. 1.—Structural formula of chlordane.

The hazard of skin absorption of chlordane preparations was the subject of studies by Ambrose and his associates.[6] These workers applied chlordane in cottonseed oil and in ethyl alcohol to the depilated skin of albino rats. The administration of chlordane in cottonseed oil by this method in amounts of 50 mg. per day for three days, or for a total dose of 217 mg. per kilogram, caused fatalities among all rats tested. Chlordane in alcohol, however, when similarly administered in like doses produced no evidence of intoxication. These findings suggest that in some, but not all, preparations of chlordane the hazard of skin absorption may be equal to that of ingestion.

Stohlman and co-workers investigated the relationship between the dose of chlordane administered to rabbits and the quantity of organic chlorine which subsequently appeared in the urine. The data of their report have been used by us for the construction of a curve (fig. 2) that

Dr. Robert M. Laughlin, to whose service the patient was admitted, gave permission to publish a report of this case.

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shows this relationship for the first 24 hour period following chlordane administration.

The effect on humans of continuous exposures to small amounts of chlordane was the subject of a report by Princi and Spurbeck,[7] who presented a clinical study of 34 workers engaged from one to three years in the manufacture and formulation of chlordane and the chemically related compounds aldrin and dieldrin. The concentrations of mixtures of these three substances in the atmosphere of the work environment were estimated on the basis of the chlorine content of the air to be somewhat in excess of 5 mg. per cubic meter. The authors assumed that there was some absorption of these compounds through the skin in addition to the obvious pulmonary route. Thorough clinical examinations of the workers thus continuously exposed did not show any relevant central nervous system, hepatic, hemopoietic, or renal changes. Although it is impossible from the data in the published paper to calculate an approximate dose that these workers might have absorbed, the study does

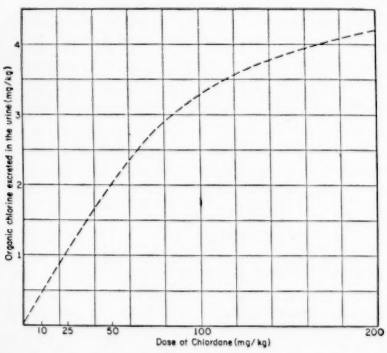


Fig. 2.—Urinary excretion of organic chlorine during the first 24 hours following administration of chlordane as a function of the dose administered to rabbits.

establish that there is some quantity of chlordane that may be taken into the body daily for at least three years without discernible ill-effect. A reasonably precise definition of this quantity needs to be established by further studies.

The published literature available to the authors contains records of two previous cases of chlordane intoxication. One of these, described by Lemmon and Pierce,[8] has been questioned as an authentic case. It occurred in a 33-year-old housewife who was exposed for an unknown number of hours in a closed room to the vapors of a 1 or 2% solution of chlordane that had previously been applied to the room surfaces for insecticidal purposes. The patient was hospitalized four days later because of nausea, vomiting, and a cough productive of whitish sputum. There was a history of alcoholism before and during the chlordane exposure. The pertinent positive findings were an enlarged liver, and abnormal results of cephalin flocculation and sulfobromophthalein (Bromsulphalein) tests. A suspicion of hepatic cirrhosis would seem to be reasonable in this case. Heyroth,[9] in a communication discussing this report, points out that the absence of any mention of the expected neurological manifestations of chlordane poisoning is good reason for doubting the assumption that chlordane was the cause of illness in this patient.

Lensky and Evans [10] reported a case of a 15-month-old baby who accidentally drank a small amount of chlordane suspension. The amount taken by this child weighing 9 kg. was believed to be not more than a mouthful (less than 100 mg.) of the suspension. Three hours after ingestion there developed a generalized tremor followed by convulsions. Risus sardonicus, opisthotonus, bilateral ankle clonus, and generally hyperactive reflexes were present. The convulsions were controlled by the use of sodium amobarbital. During the next few days only moderate ataxia and irritability remained, and these progressively diminished and disappeared after three weeks. This case strongly suggests that treatment should be immediately directed toward the removal of chlordane from the body even when the amount ingested is apparently trivial.

REPORT OF A CASE

At 7:30 a. m. on March 2, 1953 (five hours before hospital admission), an 18-year-old college girl swallowed a teaspoonful of a commercial insecticide containing 40% agricultural grade chlordane (24% chlordane and 16% related compounds), 10% oil of pine, 10% polyethylene glycol, and 40% of petroleum distillate. The patient had mistaken this preparation for camphorated opium tincture (paregoric), which she customarily took for dysmenorrhea. The mistake was discovered at once. She ate some bread and milk for its possible value as an antidote, and went to school. At 9 o'clock, one and one-half hours later, she became nauseated and vomited; at 10:30 o'clock she experienced diplopia, blurring of vision, and twitching of the extremities. About noon, while lying down at the student infirmary, she had a generalized convulsion that is said to have lasted "a few minutes," following which arrangements were made for her admission to Woman's Hospital of Pittsburgh. En route to the hospital, four and one-half hours after she had swallowed the chlordane, she vomited a second time. The vomitus was said to have contained the bread and milk eaten earlier and to have had an odor suggestive of the chlordane solution. There was no history of any previous convulsive seizure, and the systemic review was otherwise noncontributory

The physical examination revealed a normally developed, slender, white girl, weighing about 50 kg., who was apparently comfortable and able to provide the historical details save for those of the convulsive seizure, which were furnished by her sister. There was a swollen area of contusion on the right frontal region; the tongue was lacerated and ecchymotic; and there was tenderness to palpation at the costovertebral angles. The general physical and neurological examinations otherwise revealed no abnormality, save that the patient was menstruating. The admission complete blood count showed normal values, and the urinanalysis revealed the presence of albumin and cells, which were considered due to menstrual discharge. Since there was at this time no satisfactory way of computing the dose of chlordane absorbed, certain blood chemistry determinations were made for their possible value as base lines on

7. Princi, F., and Spurbeck, G. H.: A Study of Workers Exposed to the Insecticides Chlordane, Aldrin, and Dieldrin, A. M. A. Arch. Indus. Hyg. **3**: 64 (Jan.) 1951.

8. Lemmon, G. B., Jr., and Pierce, W. F.: Intoxication Due to Chlordane, J. A. M. A. **149**: 1314 (Aug. 2) 1952.

9. Heyroth, F. F.: Chlordane Poisoning, J. A. M. A. **150**: 715 (Oct. 18) 1952.

10. Lensky, P., and Evans, H. L.: Human Poisoning by Chlordane, J. A. M. A. **149**: 1394 (Aug. 9) 1952.

which to make future judgments relative to hepatic and renal functions. The blood levels of the following substances were found to be normal: nonprotein nitrogen, chlorides, carbon dioxide, sodium, potassium, calcium, total proteins, albumin, globulin, and cholesterol. Analysis of a pooled specimen of urine collected during the first 24 hours of hospitalization revealed 1 mg. of organic chlorine per 100 ml., the total amount excreted during the period being 22 mg.

After her stomach was emptied and lavaged, the patient was not permitted to take anything by mouth for 24 hours. She was given fluids intravenously to prevent superposition of dehydration and electrolyte depletion upon the action of a possible nephrotoxic agent and possibly to enhance the renal excretion of this toxin. Accordingly, she received 2,000 ml. of 10% glucose in water and 1,000 ml. of 10% glucose in saline with water-soluble vitamins intravenously during the ensuing 20 hours. During this time her urinary output was 2,230 ml. Since there was no further convulsion or nausea, a soft diet was started on the day following admission to the hospital. The costovertebral angle tenderness was no longer present after the third day, and the remainder of her hospital course was uneventful. The blood counts and urinalysis findings continued to be normal; the blood chloride level, and serum levels of sodium, potassium, and phosphate were redetermined and found normal, as was thymol turbidity; and the cephalin flocculation test was negative. The patient was discharged from the hospital on March 7, 1953, five days after admission. After her discharge she continued to do well. An electroencephalogram, performed on April 28, was normal, and visual field examinations on May 5 revealed no abnormality.

COMMENT

As with other chemical poisons, the events to be expected in a case of acute poisoning by chlordane depend upon the dose absorbed. On the advice of Lehman,[1] chlordane and its closely related compounds in a solution of technical chlordane are to be considered together in the estimation of the dose administered. The amount of chlordane ingested in the present cases is calculated on this basis to have been 40% of 4 gm., or 1.6 gm. (32 mg. per kilogram). It should be assumed that the amount actually absorbed was less than this, but how much less cannot be definitely established. In any case, the amount absorbed was sufficient to cause transient minor central nervous system changes followed by convulsions, from all of which the patient recovered spontaneously. In a case of poisoning in an infant previously reported,[10] it was necessary to administer a barbiturate for the control of convulsions. These two cases suggest that acute poisoning in man by ingestion of a single dose of chlordane results in a series of central nervous system changes that culminate in convulsions. It is likely that a dose insufficient to produce central nervous system changes is also insufficient to produce significant changes in other organ systems. On the basis of results of acute toxicity studies in animals, it may be predicted that doses large enough to produce severe convulsions will also cause hepatic necrosis. Since the administration of chlordane over prolonged periods has produced damage of the renal convoluted tubules, this change needs to be borne in mind as a possibility in cases of poisoning among humans.

It may prove possible to estimate with satisfactory accuracy the dose of chlordane absorbed from the level of organically bound chlorine in the urine. As demonstrated by the curve in figure 2, which is based upon Stohlman's data, there is a reasonably good correlation of this type in rabbits administered single doses of chlordane. If a like correlation exists for humans, then it is possible to make an estimation of the amount of chlordane retained in the present case. The 24 hour urinary excretion of organic chlorine was 22 mg. which in this 50 kg. patient was 0.44 mg. per kilogram. From the curve in figure 2 this excretory level is representative of a retained dose of 10 mg. per kilogram. The total dose retained therefore would be 10 mg. times 50, or 500 mg. of chlordane, a value that seems reasonable in consideration of the vomiting that occurred one and one-half and again four and one-half hours following ingestion of 1.6 gm. of chlordane dissolved in oil and petroleum distillate. Because of the limitations of translating animal data to humans, no estimation is offered of a probably fatal single dose of chlordane for humans, or of the relationship of the retained dose in the presently reported case to this value. The data in the present case suggest that a dose of chlordane that results in an urinary excretory value of about 0.5 mg. of organic chlorine per kilogram during the ensuing 24 hours is sufficient to cause only transitory central nervous system changes from which the patient may be expected to recover spontaneously and completely. Because of the obvious advantage of knowing the absorbed dose at the earliest possible time, it is hoped that the relationship between dose and the urinary level of organic chlorine will be more thoroughly studied in any future cases. The practical application of routinely determined urinary organic chlorine levels as an industrial hygiene control measure among workers who are regularly in contact with chlordane is strongly suggested.

Barbiturates, especially those that are detoxified in extrahepatic tissues, may be considered to have established value in the convulsive state produced by chlordane. It is possible at this time only to assume that the usual therapeutic measures effective for hepatic necrosis will be useful in the more advanced stages of poisoning. The occurrence of lower nephron nephrosis following a single dose of chlordane is not predictable from experimental data or case reports now at hand, but this serious change should always be borne in mind. The present case, as well as one previously reported, suggests that the ingestion of 10 mg. of chlordane per kilogram of body weight, and perhaps less, is an indication for gastric lavage at the earliest feasible time.

SUMMARY

A case of human intoxication with chlordane is presented in which the dose ingested was approximately 30 mg. per kilogram of body weight and the amount retained after vomiting is estimated to be 10 mg. per kilogram of body weight. Experiences with chlordane intoxication in laboratory animals and one other human case are discussed. Central nervous system changes manifested by convulsions, with or without coma, are the outstanding characteristics of acute chlordane intoxication. Measures for handling future cases are discussed and include early evacuation of stomach contents, anticonvulsive agents, and, in severe cases, such measures as may be necessary to counteract liver damage as well as possible renal tubular changes.

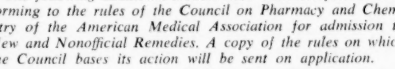
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Succinylcholine Chloride.—Anectine Chloride (Burroughs Wellcome).—Quelicin Chloride (Abbott).—$C_{14}H_{30}Cl_2N_2O_4 \cdot 2H_2O$.—M.W. 397.34.—Choline succinate dichloride dihydrate.—The structural formula of succinylcholine chloride may be represented as follows:



Actions and Uses.—Succinylcholine chloride is a myoneural blocking agent that produces a skeletal muscle relaxant effect somewhat resembling that of curare and curare-like compounds. It likewise produces muscle relaxation as an adjunct to anesthesia during surgical procedures and in conjunction with electroshock therapy. Succinylcholine chloride is a shorter-acting drug than tubocurarine chloride and, therefore, is particularly suited for endotracheal intubation, endoscopy, and other short, manipulative procedures. In contrast to tubocurarine chloride, succinylcholine chloride is not antagonized by anticholinesterases; and the injection of such drugs as physostigmine, neostigmine, procaine, or edrophonium prolongs its action. This suggests that the short action of the drug is caused by relatively rapid hydrolysis of the ester linkage by enzyme action, such as that of cholinesterases. Presumably, the drug is rapidly hydrolyzed into nontoxic choline and succinic acid and is not dependent on the liver or kidneys for detoxication or excretion.

Tachyphylaxis or cumulative action is not ordinarily encountered, but like other myoneural blocking agents, succinylcholine chloride in extremely high doses may produce respiratory depression, persisting after the diaphragmatic response to phrenic nerve stimulation has returned. Facilities for controlled, involuntary respiration and for the administration of oxygen to insure adequate respiratory exchange should be available for combating respiratory paralysis. *Neostigmine or other anticholinesterases and edrophonium are contraindicated as antidotes for succinylcholine chloride.* Succinylcholine chloride should be used with caution in patients with severe liver disease, severe anemia, and malnutrition or in those suffering from polyphosphate insecticide poisoning who may have decreased plasma-cholinesterase activity that might intensify and prolong the action of the drug. In such patients, artificial respiration and oxygen therapy may be supplemented by the administration of plasma or whole blood to restore cholinesterase activity.

Because succinylcholine chloride is rapidly hydrolyzed by alkaline solutions, it loses its potency rapidly when mixed with thiopental sodium. For this reason, separate injection is preferable.

Succinylcholine chloride is quite stable when stored under refrigeration. When exposed to room temperature for a long time, its potency gradually decreases; however, biological assay has shown that solutions may be kept as long as three months at room temperature without significant loss of potency.

Dosage.—Succinylcholine chloride is administered in solution by the intravenous route, either as a single intermittent injection or as a continuous drip infusion.

For short procedures, the suggested adult dose is 20 mg. for a single injection; the optimum dose ranges from 10 to 30 mg. Within this range each such dose usually produces relaxation in about one minute. Maximum muscular relaxation may persist for about two minutes, followed by rapid recovery within the next few minutes. Since the maximum safe dosage of the drug has not been determined, and since the response obtained may vary in different patients, careful observation of respiratory exchange is essential to avoid paralytic apnea.

For prolonged procedures, sustained relaxation may be obtained with a continuous intravenous drip infusion at a dosage rate of 0.5 mg. to 10 mg. (average 2.5 mg.) per minute for adults. The solution of the drug to be infused may be prepared by dilution of 500 mg. of succinylcholine chloride in 250 or 500 cc. of sterile isotonic sodium chloride solution or 5% dextrose solution, thus providing a 0.1% (1 mg. per cubic centimeter) or a 0.2% (2 mg. per cubic centimeter) solution, respectively. The degree of relaxation can be altered in approximately 30 seconds by regulating the rate of the drip infusion. Careful supervision of the infusion and the control of respiration are absolutely essential to avoid hypoxia.

Tests and Standards.—

Physical Properties: Succinylcholine chloride is a white, odorless, slightly bitter powder, m.p. of the hydrate, 156-163°. It is very soluble in water, very slightly soluble in benzene and chloroform, and practically insoluble in ether. The amount which dissolves in alcohol to form 100 ml. of solution is 0.42 gm. Aqueous solutions of succinylcholine chloride are relatively unstable at room temperature. The pH of a 2% solution is 3.0-4.5.

Identity Tests: Dissolve about 50 mg. of succinylcholine chloride in 10 ml. of water and divide the solution into two portions. To one portion add 2 drops of nitric acid and 1 ml. of silver nitrate T.S.: a white precipitate forms, which is insoluble in diluted nitric acid, but soluble in diluted ammonia solution *(presence of chloride).* To the second portion add 10 ml. of saturated picric acid and 2 drops of diluted sulfuric acid. Place the mixture in a refrigerator for 1 hour. Filter the mixture, wash the precipitate thoroughly with ether, and dry it at 105° for 15 min. *(Caution! May be explosive. Use safety glass shield.):* the crystals melt at 155-159°.

Purity Tests: Dissolve 0.1 gm. of succinylcholine chloride in enough water to make 25 ml. of solution, add 1 ml. of barium chloride T.S., shake, and allow the mixture to stand for 1 min.: the turbidity does not exceed that of 0.2 ml. of 0.02 *N* sulfuric acid diluted to 25 ml. and treated in the same manner *(presence of sulfate).*

Dry about 1 gm. of succinylcholine chloride, accurately weighed, in a vacuum at 105° for 5 hours: the loss in weight does not exceed 10.0%.

Char about 1 gm. of succinylcholine chloride, accurately weighed, cool the residue, add 1 ml. of sulfuric acid, heat cautiously until evolution of sulfur trioxide ceases; ignite, cool, and weigh: the residue does not exceed 0.1%.

Assay: (Succinylcholine Chloride) Transfer to a 100 ml. beaker an amount of powder equivalent to about 0.2 gm. of anhydrous succinylcholine chloride, accurately weighed, and dissolve it in 50 ml. of recently boiled and cooled water. Potentiometrically adjust the pH to 7.5 with 0.01 *N* sodium hydroxide and transfer the solution to a 300 ml. flask. Add exactly 20 ml. of 0.1 *N* sodium hydroxide, reflux for 40 min., and cool. Transfer the solution to a 250 ml. beaker and potentiometrically titrate the excess alkali with 0.1 *N* hydrochloric acid to a pH of 7.5. Run a blank titration using 50 ml. of recently boiled and cooled water. Each milliliter of 0.1 *N* sodium hydroxide consumed is equivalent to 0.01807 gm. of anhydrous succinylcholine chloride. The amount of anhydrous succinylcholine chloride is not less than 98.5 nor more than 101.5%.

(Chloride) Transfer to a 250 ml. Erlenmeyer flask about 0.3 gm. of anhydrous succinylcholine chloride, accurately weighed. Add 100 ml. of water and 1 ml. of potassium chromate T.S. Titrate with 0.05 *N* silver nitrate. Each milliliter of 0.05 *N* silver nitrate is equivalent to 0.001773 gm. of chloride and 0.009033 gm. of anhydrous succinylcholine chloride. The amount of chloride is not less than 19.2 nor more than 20.0%, equivalent to not less than 98.0 nor more than 102.0% of succinylcholine chloride.

Dosage Forms of Succinylcholine Chloride

SOLUTIONS. *Physical Properties:* The pH of the 2% and 5% solution is 3.0-4.5.

Identity Tests: The solution responds to the identity tests for the active ingredient in the monograph for succinylcholine chloride.

Assay: (Succinylcholine Chloride) Transfer to a 125 ml. separatory funnel an amount of solution, accurately measured, equivalent to about 0.2 gm. of anhydrous succinylcholine chloride. Add 40 ml. of recently boiled and cooled water, extract with five 25 ml. portions of ether, and combine the extracts in a 250 ml. separatory funnel. Wash the extracts with three 5 ml. portions of water. Discard the ether extracts and reextract the combined wash solutions with two 10 ml. portions of ether, adding the aqueous phase to the extracted aqueous solution. Proceed as directed in the assay for succinylcholine chloride in the monograph for succinylcholine chloride starting with, "Potentiometrically adjust the pH to 7.5 . . ." Each milliliter of 0.1 *N* sodium hydroxide consumed is equivalent to 0.01807 gm. of anhydrous succinylcholine chloride. The amount of anhydrous succinylcholine chloride is not less than 92.5 nor more than 107.5% of the labeled amount calculated to the anhydrous basis.

Abbott Laboratories, North Chicago, Ill.

Solution Quelicin Chloride: 10 cc. vials. A solution containing 20 mg. of succinylcholine chloride in each cubic centimeter. Preserved with 0.18% methylparaben and 0.02% propylparaben.

Solution Quelicin Chloride: 10 cc. ampuls. A solution containing 50 mg. of succinylcholine chloride in each cubic centimeter.

Burroughs Wellcome & Company, Inc., Tuckahoe, N. Y.

Solution Anectine Chloride: 10 cc. vials. A solution containing 20 mg. of succinylcholine chloride in each cubic centimeter. Preserved with 0.1% methylparaben.

Solution Anectine Chloride: 10 cc. ampuls. A solution containing 50 mg. of succinylcholine chloride in each cubic centimeter.

p-Aminosalicylic Acid (See New and Nonofficial Remedies 1953, p. 89).

Sharp & Dohme, Division of Merck & Co., Inc., Philadelphia.

Effervescent Tablets Propasa: 1 gm. Each tablet contains 1 gm. of *p*-aminosalicylic acid and 0.7 gm. of sodium bicarbonate. When dissolved in water each tablet yields 1.38 gm. of sodium *p*-aminosalicylate.

Ascorbic Acid-U.S.P. (See New and Nonofficial Remedies 1953, p. 502).

Rexall Drug Company, Los Angeles.

Tablets Ascorbic Acid: 25 and 50 mg.

Benzethonium Chloride (See New and Nonofficial Remedies 1953, p. 81).

Chemo Puro Manufacturing Corporation, Long Island City, N. Y.

Powder Benzethonium Chloride: Bulk; for manufacturing use.

Choline Gluconate (See New and Nonofficial Remedies 1953, p. 445).

Chemo Puro Manufacturing Corporation, Long Island City, N. Y.

Solution Choline Gluconate: Bulk; for manufacturing use. A solution containing 0.58 to 0.62 gm. of choline gluconate in each cubic centimeter.

Ethinyl Estradiol (See New and Nonofficial Remedies 1953, p. 362).

Chemo Puro Manufacturing Corporation, Long Island City, N. Y.

Powder Ethinyl Estradiol: Bulk; for manufacturing use.

Ethyl Iodophenylundecylate (See New and Nonofficial Remedies 1953, p. 288).

Lafayette Pharmacal, Inc., Lafayette, Ind.

Emulsion Pantopaque, 50% V/V: 10 cc. ampuls. An emulsion containing 0.5 cc. of ethyl iodophenylundecylate in each cubic centimeter. U. S. patent 2,348,231. U. S. trademark 401,476.

Gamma Benzene Hexachloride (See New and Nonofficial Remedies 1953, p. 73).

Chemo Puro Manufacturing Corporation, Long Island City, N. Y.

Powder Gamma Benzene Hexachloride: Bulk; for manufacturing use.

Hexamethonium Chloride (See New and Nonofficial Remedies 1953, p. 241).

Chemo Puro Manufacturing Corporation, Long Island City, N. Y.

Powder Hexamethonium Chloride: Bulk; for manufacturing use.

Isoniazid (See New and Nonofficial Remedies 1953, p. 85).

Hoffmann-LaRoche Inc., Nutley, N. J.

Tablets Rimifon: 50 and 100 mg. U. S. patent 2,596,069. U. S. trademark 563,939.

Mephenesin (See New and Nonofficial Remedies 1953, p. 466).

American Pharmaceutical Company, New York.

Tablets Mephenesin: 0.25 and 0.5 gm.

Gold Leaf Pharmacal Company, Inc., New Rochelle, N. Y.

Tablets Mephenesin: 0.5 gm.

Methapyrilene Hydrochloride (See New and Nonofficial Remedies 1953, p. 9).

Chemo Puro Manufacturing Corporation, Long Island City, N. Y.

Powder Methapyrilene Hydrochloride: Bulk; for manufacturing use.

Neostigmine Bromide-U.S.P. (See New and Nonofficial Remedies 1953, p. 182).

Hoffmann-LaRoche, Inc., Nutley, N. J.

Ophthalmic Solution Prostigmin Bromide 5%: 7.5 cc. dropper bottles. A solution containing 50 mg. of neostigmine bromide in each cubic centimeter. Buffered with 1% boric acid. Preserved with 0.18% methylparaben and 0.02% propylparaben.

Neostigmine Methylsulfate-U.S.P. (See New and Nonofficial Remedies 1953, p. 182).

Lincoln Laboratories, Inc., Decatur, Ill.

Solution Neostigmine Methylsulfate 1:2000: 10 cc. vials. Preserved with 0.45% phenol.

Pentaerythritol Tetranitrate (See New and Nonofficial Remedies 1953, p. 244).

Chemo Puro Manufacturing Corporation, Long Island City, N. Y.

Powder Pentaerythritol Tetranitrate: Bulk; for manufacturing use. A mixture containing 75 mg. of pentaerythritol tetranitrate in each gram of powder.

Progesterone-U.S.P. (See New and Nonofficial Remedies 1953, p. 376).

Gold Leaf Pharmacal Company, Inc., New Rochelle, N. Y.

Solution Corlutone in Oil: 1 cc. ampuls and 10 cc. vials. A solution in sesame oil containing 10 and 25 mg. of progesterone in each cubic centimeter. The 10 cc. vials are preserved with 0.5% chlorobutanol.

Pyridoxine Hydrochloride-U.S.P. (See New and Nonofficial Remedies 1953, p. 493).

American Pharmaceutical Company, New York.

Tablets Pyridoxine Hydrochloride: 10 and 25 mg.

Pyrilamine Maleate (See New and Nonofficial Remedies 1953, p. 12).

The Columbus Pharmacal Company, Columbus, Ohio.

Tablets Pyramal Maleate: 50 mg.

Riboflavin-U.S.P. (See New and Nonofficial Remedies 1953, p. 496).

Hart Drug Corporation, Miami, Fla.

Tablets Riboflavin: 5 and 10 mg.

Sodium *p*-Aminosalicylate (See New and Nonofficial Remedies 1953, p. 91).

Chemo Puro Manufacturing Corporation, Long Island City, N. Y.

Powder Sodium Para-Aminosalicylate: Bulk; for manufacturing use.

Merck & Company, Inc., Rahway, N. J.

Powder Sodium Para-Aminosalicylate: 500 gm. bottles and 2.5, 11.35 and 45.4 kg. fiber drums; for manufacturing use.

Sodium Dehydrocholate (See New and Nonofficial Remedies 1953, p. 337).

Lincoln Laboratories, Inc., Decatur, Ill.

Solution Sodium Dehydrocholate: 10 cc. ampuls. A solution containing 0.2 gm. of sodium dehydrocholate in each cubic centimeter.

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CHLOROPHYLL AND DEODORIZATION

There was published in THE JOURNAL [1] an editorial entitled "Chlorophyll as a Deodorant." This precipitated considerable correspondence, some of which came from those with interests in the commercial possibilities for preparations containing chlorophyllins. Some of the correspondents questioned some of the statements made in the editorial, some referred to articles published elsewhere that they believed offered convincing evidence of the value of chlorophyll or its derivatives as a deodorant. For several years there has been accepted by the Council on Pharmacy and Chemistry of the American Medical Association a chlorophyllin-type preparation that is promoted only to the medical profession and with claims recognized by the Council. No other preparations stand accepted by the Council, and the evidence for the claimed usefulness of chlorophyll toothpastes, mouthwashes, chewing gum, tablets to be taken by mouth, and other similar concoctions seems to be wanting or at least open to dispute. As THE JOURNAL editorial pointed out, "It seems apparent that no final conclusion can be reached about the deodorizing effects of chlorophyll derivatives until the composition of the various preparations is more exactly delineated, the fate of ingested chlorophylls in the body is determined, and more objective testing has been done."

Elsewhere in this issue (page 745) is reproduced some of the correspondence received in the editorial office. This had barely been accepted by the Editor when there was published in a local newspaper (Sept. 30) an Associated Press release on a panel discussion at the annual meeting of the American Dental Association. According to the release, one of the participants in the panel said "claims that toothpastes containing chlorophyll can give a deodorizing effect for several hours should be viewed with suspicion." So far there appears to have been no official denial of such a statement by organized dentistry, and it is presumed, therefore, that the incorporation of chlorophyll derivatives in toothpastes is open to suspicion as far as claims are concerned. Other information reaching THE JOURNAL office indicates validity of THE JOURNAL'S earlier assertion that there is need for conclusive evidence before many of the claims offered for this type of preparation and others sold widely to the public can be accepted without any suspicion.

1. J. A. M. A. **152**: 1716 (Aug. 29) 1953.

SURGICAL SURVIVAL OF THE YOUNG AND THE AGED

Although operations performed on elderly patients under most circumstances are more hazardous than when done on young patients, Cole [1] points out that it is not generally realized that, if concurrent and complicating diseases are eliminated, aged patients will tolerate operative procedures of moderate magnitude almost as well as the young. Few will dispute the statement that the reserve of certain body functions and organs decreases with the passing of time. There is, for instance, reliable evidence to demonstrate that the elasticity of arteries and arterioles decreases with age; consequently, elderly persons are more susceptible to vascular shock than young persons. Similarly, arteriosclerotic changes in the vascular supply of the kidney make the elderly patient especially vulnerable to renal dysfunction, while degenerative vascular changes probably explain why older persons tolerate heat and cold so poorly. Moreover, elderly patients are more susceptible than the young to anoxia and to infections. As a result of these changes, it is to be expected that older patients will have a lower physiological reserve to combat major operations.

In order to determine the mortality rate of patients less than 60 years of age as compared to patients over 60, Cole made a survey of 3,656 major operations that were performed by members of the general surgical service at the Illinois Research Hospital from 1948 to 1952 inclusive. He limited the study to patients subjected to various types of abdominal, thoracic, vascular, plastic, urologic, breast, extremity, and neck surgery. Radical excision of the breast, thyroidectomy, and all types of herniorrhaphy were considered major operations. The majority of abdominal and thoracic procedures consisted of operations for inoperable carcinoma, with most colostomies, gastrostomies, and radical oral and neck operations performed for this disease. In addition, such procedures as pulmonary lobectomies, suprapubic and retropubic prostatectomies, enteroenterostomies, and pancreatectomy came within the scope of the survey.

Cole concluded that there is an accumulation of evidence to demonstrate that if the operative load lies within certain limits and if elderly patients are rendered free from concurrent disease, the mortality rate of the aged in major operations of slight magnitude is almost equal to that found in younger patients, provided, of course, all decrements and insufficiencies are met before operation and excellent postoperative care is instituted. Contrariwise, in the case of operations of greater magnitude, the mortality rate to be expected in the older group may be two to four times higher than in the younger group. A survey of reports appearing in the medical literature indicates that the mortality rate encountered as the result of emergency operations performed on the aged is substantially higher than in elective surgical procedures. The Illinois Research Hospital study also demonstrated that the mortality rate following radical excision of the breast, cholecystectomy, gastrectomy, herniorrhaphy, and thyroidectomy was no higher in patients over 60 years of

1. Cole, W. H.: Operability in the Young and Aged, Ann. Surg. **138**: 145 (Aug.) 1953.

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age than in patients under 60. The mortality rate in 2,577 operations performed on patients under 60 at this institution was 2.07% as compared to 5.1% in 1,099 patients over 60 years of age.

DIAGNOSIS OF MITRAL REGURGITATION

Estimation of the degree of mitral insufficiency in candidates for mitral commissurotomy is of considerable importance. While mild to moderate regurgitation need not significantly effect the outcome, severe regurgitation is a contraindication to the procedure.[1] With a view to evaluating criteria commonly used for diagnosing mitral regurgitation, Abelmann, Ellis, and Harken [2] have correlated the clinical findings in candidates for valvuloplasty with pathological anatomic observations made at surgery or at autopsy. Sixty-four persons in all were studied. In 62 of these some degree of mitral stenosis was found at operation. Twenty-seven were found at operation to have some degree of mitral regurgitation, which was graded according to the size and force of the regurgitant jet as felt by the surgeon's finger. One was found to have pure mitral insufficiency at operation, and in one the diagnosis of pure mitral insufficiency suspected during life was confirmed at death, which occurred before surgical correction was attempted. The following criteria were examined: the apical systolic murmur, the symptom of easy fatigability, enlargement of the left ventricle, absence of electrocardiographic pattern of right ventricular enlargement or right bundle branch block, marked enlargement of the left auricle, systolic expansion of the left auricle as assessed by fluoroscopy, the auricular esophagogram, the auricular border electrokymogram, and the phonocardiogram.

It was found that the most valid criteria for the diagnosis of marked mitral regurgitation were the presence of a loud apical systolic murmur, marked left auricular enlargement, left ventricular enlargement, and systolic expansion of the left auricle by fluoroscopy. Thus, of 14 patients with apical murmurs of grade 3 or louder, 6 showed severe regurgitation at operation, 4 showed mild to moderate regurgitation, and 4 showed no regurgitation. On the other hand, of 23 patients without systolic murmurs, there was no regurgitation in 15, it was questionable in 7, and it was moderate in 1. Again, of nine patients with marked regurgitation, six had markedly enlarged left auricles and three had moderate enlargement only. Contrariwise, of 45 patients with slight or moderate enlargement, 29 had pure stenosis, 13 had questionable to moderate regurgitation, and only 3 had marked regurgitation. Of 15 patients showing definite left ventricular enlargement by either electrocardiogram or roentgen examination, all but 2 showed mitral regurgitation; however, failure to demonstrate left ventricular enlargement does not rule out mitral regurgitation, since 8 patients with moderate to severe regurgitation did not show definite evidence of left ventricular enlargement.

In regard to systolic expansion of the left auricle as observed fluoroscopically, of 48 patients who were subjected to fluoroscopic studies, 33 showed definite expansion of the left auricle. Seven of 8 patients with marked regurgitation fell in this category while in the eighth patient expansion was questionable. However, 7 of 17 patients without demonstrable regurgitation also showed systolic expansion.

In 47 patients on whom all four of the above tests were run, it was found that any two of the four criteria were met by 5 of 7 patients with marked regurgitation, by 12 of 19 patients with mild to moderate regurgitation, by 1 of 4 patients with questionable regurgitation and by only 1 of 17 patients with pure stenosis.

In regard to the other criteria, fatigability overshadowing dyspnea was observed in nine patients, only four of whom show regurgitation to a moderate to marked degree. While it is claimed that the absence of electrocardiographic evidence and right ventricular hypertrophy in patients with mitral disease suggests the presence of both stenosis and regurgitation, Abelmann and his associates report that 15 of the 32 patients with no evidence of bundle branch block or right ventricular hypertrophy by electrocardiogram showed no evidences of mitral regurgitation at valvuloplasty while 11 showed only questionable or mild insufficiency, which indicates that such patterns are not restricted to patients with both stenosis and regurgitation. Studies with auricular esophagograms confirmed the existence of an esophageal auricular pressure pulse characteristic for mitral regurgitation but proved too sensitive a method to quantitate mitral regurgitation. In fact, the presence of this pattern in many patients in whom no regurgitant jet was felt by the surgeon tends to confirm the viewpoint that mitral stenosis is almost invariably accompanied by some degree of regurgitation. Abelmann and co-workers also found left auricular border electrokymography disappointing, patterns reportedly characteristic of mitral regurgitation being found in all patients with mitral disease and in many patients without heart disease, while phonocardiogram results appeared to be too inconstant to be of any diagnostic value.

The authors conclude from these studies that no single criterion is adequate for the preoperative diagnosis of severe mitral regurgitation in patients with mitral stenosis. They feel, however, that consideration of all clinical findings usually permits assessment of the individual patient. Thus the presence of a systolic murmur of grade 2 or less, a left auricle moderately enlarged in posterior direction only, evidence of right ventricular enlargement by roentgenogram or electrocardiogram without evidence of left ventricular enlargement, and the finding of definite but slight systolic posterior expansion of the left auricle by fluoroscopy, kymogram, or esophagogram suggest that mitral insufficiency of a degree to contraindicate cardiac surgery is not present. On the other hand, definite evidence of left ventricular enlargement, associated with other presumptive signs of regurgitation, such as a loud systolic murmur, marked left auricular enlargement with systolic expansion, and fatigability rather than dyspnea are suggestive of mitral insufficiency sufficiently advanced to render exploratory cardiotomy inadvisable.

1. Janton, O. H.; Glover, R. P., and O'Neill, T. J. E.: Indications for Commissurotomy in Mitral Stenosis, Am. J. Med. **12**: 621, 1952. Bland, E. F.: Surgery for Mitral Stenosis: A Review of Progress, Circulation **5**: 290, 1952. Harken, D. E., and others: Responsibility of Physician in Selection of Patients with Mitral Stenosis for Surgical Treatment, ibid. **5**: 349, 1952.

2. Abelmann, W. H.; Ellis, L. B., and Harken, D. E.: Diagnosis of Mitral Regurgitation: An Evaluation of Clinical Criteria, Fluoroscopy, Phonocardiogram, Auricular Esophagogram, and Electrokymogram, Am. J. Med. **15**: 5, 1953.

ORGANIZATION SECTION

STATEMENT BY EDWARD J. McCORMICK ON MEDICAL RESEARCH AND PROGRESS BEFORE HOUSE COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE

I am Dr. Edward J. McCormick of Toledo, Ohio, where I am engaged in the active practice of medicine. I am President and a member of the Board of Trustees of the American Medical Association. I am appearing here today as a representative of that Association to discuss our interest and activities in the field of medical research and to offer to your Committee our complete cooperation and the use of our facilities in connection with your current inquiry.

It is our understanding that this hearing has been initiated by your Committee for the purpose of studying the causes, methods of control and the extent of medical progress in connection with several specific diseases. It is apparent from the list of organizations which are scheduled to testify that complete and authentic information in this regard will be available to you. For that reason it has been decided, with the approval of Mr. John H. Teeter, Special Consultant to your Committee, not to present a separate statement with respect to each of the diseases to be covered. In addition to my statement, a representative from the Washington office of the American Medical Association will be in attendance for the entire hearing. If there are any questions which the Committee may want to direct to the Association, our representative will either supply the answer or refer the request to our headquarters in Chicago for necessary action. Finally, at the conclusion of the initial phase of the hearings we will be happy to submit a written statement or send another witness to discuss in detail any controversial issues which may arise. It is our belief that this approach will conserve the time of the Committee and prevent duplications in the presentation of basic material.

The one exception to this plan will be made tomorrow when the subject of cancer is to be discussed. In view of the extensive work of the American Medical Association in this field, I have asked Dr. Paul Wermer, the Secretary of our Committee on Research, to outline for you the activities of the Association concerning cancer diagnosis, treatment and research.

With these introductory remarks I should like to proceed to a brief statement concerning the composition, purposes and program of our Association.

The American Medical Association was founded on May 5, 1847, when 250 delegates representing more than 40 medical societies and 28 colleges, embracing medical institutions in 22 states and in the District of Columbia, met in Philadelphia, Pennsylvania. It has since grown from an organization of a few thousand to a membership of approximately 140,000, with 53 constituent state and territorial medical associations and about 2,000 component county and district medical societies.

The American Medical Association is a physician's organization existing to serve the medical profession and the general public. Since its inception it has campaigned to elevate the standards of medical education, licensure and public health; to maintain its high ethical standards; to oppose charlatanism; to promote clinical and scientific investigation, and to make available a better quality of medical service.

Although the American Medical Association acts collectively for physicians in the socio-economic field of medicine, which includes ethics, laws and legislation, medical service, economic research, rural health and health education, primary emphasis is placed on its scientific activities.

During the year 1952 over 80% of our expenditure of approximately $10,000,000 was devoted to this work. These activities are conducted largely by the Council on Medical Education and Hospitals, the Council on Scientific Assembly, the Bureau of Exhibits, the Committee on Mental Health, the Council on Pharmacy and Chemistry, Council on Physical Medicine and Rehabilitation, Council on Foods and Nutrition, Committee on Cosmetics, Committee on Research, Bureau of Investigation, and the Chemical Laboratory and Microbiologic Laboratory.

It would take considerable time for me to discuss in any detail the purposes and programs of these units of our Association. Suffice it to say that all of their work is extremely important in advancing the science of medicine. The outstanding reputation of the members of these Councils and Committees for specialized scientific knowledge and integrity is well recognized. These men serve without remuneration and render unbiased decisions based on careful considerations of all available scientific evidence and expert opinion.

Through The Journal of the American Medical Association, published weekly, and the nine monthly scientific journals, as well as several special books, the Association aids physicians in their search for new medical knowledge. These publications assist the medical profession in keeping abreast of medical developments, serve as an important means of postgraduate medical education and carry information on organization activities, as well as on government services.

In addition to such inter-Association groups, the American Medical Association has for many years engaged in a variety of cooperative undertakings with allied health agencies as well as with the state and federal governments. The operations of three such joint agencies which are currently in existence may be of interest to your Committee.

The National Research Council.—This agency was established in its present form in 1916 by the National Academy of Sciences and organized with the cooperation of the National Scientific and Technical Societies of the United States. Its purpose is to promote research in the natural sciences and in their application to medicine and other useful arts with the object of increasing knowledge, strengthening the national defense and contributing in other ways to the public welfare. To this end the Council furnishes professional and research advice to governmental and other organizations and administers such funds as may be entrusted to it.

The American Medical Association maintains liaison with the National Research Council through representation on the Division of Medical Sciences and the Food and Nutrition Board. In this capacity we are able to assist and cooperate in the effective prosecution of the Council's work.

The Commission on Chronic Illness.—This Commission was founded in 1949 as a non-profit organization by the American Medical Association, the American Hospital Association, the American Public Health Association and the American Public Welfare Association. At the present time 12 national organizations contribute financially and professionally to the program of the Commission.

Studies of the Commission include those to determine the prevalence and incidence of the major chronic diseases and how many and what services are needed; studies to determine effective means of prevention, rehabilitation and care; fact finding projects to learn what services and facilities are now available and what kinds of planning are going on.

Briefly, it can be stated that the goals of the Commission are to define the problems arising from chronic illness in all age groups; pave the way for dynamic programs to prevent chronic illness, minimize its disabling effects, restore its victims to a socially useful and economically productive place in the community; clarify the interrelationships of the many professional groups and agencies working in the field; coordinate the separate programs designed to meet more effectively the needs common to all the chronically ill; stimulate in every locality a well-rounded plan for the prevention and control of chronic disease and for the care and rehabilitation of the chronically ill; and modify society's attitude that chronic illness is hopeless.

Committee on Relations Between Medicine and Allied Health Agencies.—In June 1952 the House of Delegates of the American Medical Association authorized this Committee for the purpose of establishing better coordination and understanding between voluntary health agencies. It was also the intention of the House of Delegates to encourage the development of case finding methods, in the office of physicians, which would be more effective than the mass surveys employed by most public and private agencies.

Now, a word about medical programs in general. The advances of medical science since the beginning of the twentieth century offer convincing evidence of what can be done when competent researchers have an opportunity to work with freedom, facilities and funds. A review of the medical discoveries since the turn of the century would require volumes. Drugs and operations, for example, alone could provide endless material for discussion of the onward march of medical research. Insulin, vitamins, sulfonamides, penicillin and other antibiotics are only a few of the outstanding discoveries in the drug field. Isotopes and betatrons have become part of the medical language. Even entirely new approaches to illness have been discovered, as a result of which, the full possibilities of formerly practically unknown subjects such as physical medicine and rehabilitation are being explored with a thoroughness that offers much promise for the future. Truly, the past fifty years have been remarkable for those who devote their lives to the prevention of illness and the treatment of the sick.

The decline in the general mortality rate from 17.2 deaths per 1,000 population in 1900 to only 9.6 in 1950 underscores the health progress during this period. While the population has doubled, the number of persons over 65 years of age has quadrupled in this period and a significant gain in life expectancy, even in late middle age, has resulted from the mortality reduction. Life expectancy at birth in 1900 was estimated at 47.3 years; in 1949 it was 67.6 years.

Major mortality gains have resulted from preventive medicine and the development of specific cures. Preventive medicine has been successful in eliminating, in a large measure, the spread of disease. Medical research has developed many effective methods of immunization and disease prevention; these have been widely used by public health agencies and sanitary engineers under the capable guidance and direction of the medical profession.

In conclusion, I should like to say that the American Medical Association will continue to support all programs for the good of the health of the public, as we have done over the years. We shall fight, however, with all of our strength, matters that are not in the public interest. Our Association has, throughout its history, been a champion of sound progress in medicine. It has had to fight many battles against quackery, improper governmental interference and against slipshod medical training and practice. We have found that an organization cannot be strong and fearless in defending its principles without creating bitter enemies and staunch supporters. We have both today.

This concludes my formal statement. I want to thank the Committee for allowing our Association an opportunity to participate in these important hearings. I shall be happy to answer to the best of my ability any questions which members of the Committee may have.

STATEMENT BY PAUL WERMER ON CANCER DIAGNOSIS, TREATMENT, AND RESEARCH BEFORE HOUSE COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE

I am Dr. Paul Wermer of Chicago, Illinois. For six years I was a practicing physician in New York City. Thereafter I served for five years in the United States Public Health Service, after which I spent four years in clinical research work in the pharmaceutical industry. Since 1949 I have been the Secretary of the Committee on Research of the Council on Pharmacy and Chemistry of the American Medical Association. I am appearing here today as a representative of that Association to outline our activities in the field of cancer diagnosis, treatment and research.

As Dr. Edward J. McCormick indicated in his statement yesterday, the American Medical Association includes in its membership physicians from all walks of professional life and is interested and engaged in a variety of activities. Thus, cancer, while absorbing, does not represent the Association's sole interest in the fight against diseases and death. In line with the schedule of the Committee, I will limit my remarks today to the field of cancer. I will also attempt to avoid repeating information dealing with the description of the disease, its causes and general research data which has been covered by other witnesses.

I should like however, to emphasize our realization of the extreme seriousness of this particular disease. Obviously, a malady which is in second place among the causes of death is a matter of pressing concern not only to organized medicine but to every member of the profession. To each physician, whether family advisor or specialist, every death resulting from cancer is a defeat for scientific medicine. Thus, all of us are vitally interested in ascertaining the solution to this problem. We believe that this answer must be found by further education and research. In this manner we hope to determine the causes, the earliest method of diagnosis, the best treatments and the best methods for early determination of a patient's response to treatment.

In the field of cancer diagnosis, treatement and research, the American Medical Association plays a prominent professional educational role. The Journal of the American Medical Association is prepared and distributed weekly to close to 150,000 practicing physicians. During the year ending Sept. 26, 1953, THE JOURNAL published 21 articles and clinical notes, 156 abstracts of articles appearing in domestic and foreign medical journals, and answered a number of inquiries from domestic and foreign correspondents on the subject of cancer. In addition, THE JOURNAL has commented editorially on cancer in six of the 52 issues represented in this survey.

In addition, the Association publishes nine special journals monthly, each of which has carried several articles on cancer in the special areas of interest.

At the Annual Meeting of the American Medical Association in New York City this past June, there were 31 scientific papers and 25 scientific exhibits on cancer. In addition, there were two nation-wide television programs and five motion pictures shown to the visiting physicians dealing with this disease. The meeting was visited by approximately 18,000 practicing physicians and over 5,000 students, interns and technicians.

By these educational devices (our publications and our meetings) the American Medical Association brings to the readers of its journals and to its membership, the latest advances in acceptable methods of therapy and diagnosis. Editorially, we repeatedly emphasize to our members the need to be constantly alert to the possibility of the existence of cancer in their patients regardless of age, and the necessity for the earliest possible diagnosis of malignancy. It is axiomatic that the earlier the diagnosis the more effective are our means of combating cancer with surgery, x-ray and radium. To this end, in 1952 a series of six articles was sponsored by our Committee on Research. These articles were solicited from leading cancer specialists and were designed to encourage the application of some of the latest methods for early cancer diagnosis in office practice.

At this junction I would like to note that so far I have been outlining solely the accomplishments of the American Medical Association in this professional educational field. By no means do I wish to imply that we are alone in carrying out this task. On the contrary, we are ably joined by the local and state medical societies which make significant contributions in this regard. The state and local medical societies in their publications and regular meetings include many discussions, articles, and papers on cancer. Each hospital's medical staff holds conferences and meetings on cancer and other medical problems.

Outside of our Association and affiliated groups, the American Cancer Society and its subsidiary state and local societies, as well as the National Cancer Institute, the Damon Runyan Foundation and special societies of both lay and professional people too numerous to mention join in this task.

The Association has been equally interested in the field of cancer research. For the past six years we have supported, with the cooperation of representatives of the drug industry, a far reaching survey of the effects of certain sex gland hormones and allied substances upon the course of various forms of cancer. We became interested in this program because it offered promise of a method of treatment, within the skill of most physicians, which would permit office or home care for the long-term cases of inoperable cancer of the breast, prostate gland and possibly other organs.

In 1946 when this program was inaugurated only a few breast cancer cases, treated with these endocrine substances, had been reported upon. It was imperative to learn as quickly as possible the efficacy of these agents, the best dosages and possible hazards in this therapy. It was obvious that no one physician or clinic could see enough cases in a relatively short period of time to accurately assess the problems outlined. It was equally obvious that if the benefits of this treatment were to devolve to patients suffering from cancer as quickly as possible, it was necessary to organize a cooperative study involving many clinics and investigators.

The Subcommittee on Steroids and Hormones of the Committee on Research undertook the organization and conduct of such a study. It is not my intention to comment on the mass of data which has been accumulated; however, certain pertinent facts concerning this study deserve mention. In all, 45 clinics and 65 investigators joined in the task. They deserve the majority of the credit for the results achieved. The pharmaceutical industry has also been extremely cooperative in supplying large quantities of expensive and, in some instances, rare substances for distribution through the Committee to investigators without charge. The American Medical Association bore all of the administrative costs plus the costs for biennial meetings including travel of all investigators.

This subcommittee was faced with problems of standardizing as far as possible the selection of proper patients for treatment in the various clinics. From their own experience, the members devised varying dosage schedules and designated the clinics which would use them. The investigators were furnished with standard forms so that their reports would be as uniform as possible. These reports were filed quarterly and the data was analyzed by the office staff of the Committee on Research in Chicago. Thus, in a relatively short time the medical profession was in possession of definite criteria for the selection of patients for this form of treatment plus definite dosage schedules which met the needs of the majority of their patients. In this way the dangers inherent in the therapy were also discovered in advance. This was accomplished by seven Committee publications in The Journal of the American Medical Association and approximately 100 individual publications.

It may be of interest to the Committee to know that over 2,000 inoperable breast cancer cases have been registered and treated. At the present moment an analysis of the total data accumulated is in progress with a view to the publication of the results as a series of monographs. Currently substances are being tested in the hope of finding more effective compounds with fewer side-effects. The studies themselves have been widened to include cancer of the female and male sex organs, the urinary bladder, the thyroid gland, and certain bone tumors. We should like to emphasize that each of our investigators is still a free agent. They are not bound rigidly to our organization. Each is free to conduct other research projects for other agencies even upon the forms of cancer in which we are primarily interested. All we ask of the collaborating investigators is that they report their results to our central office. These results are then disseminated among other investigators by means of bulletins and letters. Thus, it may be seen that the primary efforts of the American Medical Association as well as those of many other medical societies is towards the expeditious exchange of scientific and objective medical information.

The road to the solution of the cancer riddle is not an easy one since we know little about the actual cause or causes of this group of diseases. It is also unfortunate that all the problems in regard to cancer are not on the positive side, that is, imposed by the disease. There is instead a venal, negative side, with problems which are man made, created by those who seek commercial gains by foisting false hopes and cures on the cancer patient and his family. For over half a century the American Medical Association has shown bold leadership in opposing these forces. During this time we have maintained an agency for the collection and dissemination of information on nostrums and quackery. We feel this task to be a public duty in order to protect the laity and to furnish physicians with objective evidence as to the lack of value and the identity of the secret nostrums proposed as cures.

In this endeavor the Association, through its Bureau of Investigation, has cooperated closely with the various federal and state agencies charged with the enforcement of laws regulating the drug industry. We have also cooperated with the state agencies which have jurisdiction over the licensing of individuals who seek to follow either the practice of medicine or the other healing arts.

In turning the searchlight of truth upon these cancer quacks we have frequently become the defendant in a court of law. Thus, the Association has been obliged to spend large sums of money in the defense of such legal actions. It is significant, however, to note that although we have been sued for more than 40 million dollars over the years, we have been obliged to pay but one judgment and that, in the nominal sum of one penny.

This is a constant battle in which we have chosen to remain in the forefront. Even now several nostrums are being promoted to the public either on representation that cures are obtainable or that the proponents are experimenting clinically with something new and valuable in the management of cancer patients, particularly those beyond the conventional methods of treatment used by medicine.

In our efforts to educate and expose, we have been joined by the American Cancer Society, the National Cancer Institute, the Damon Runyan Foundation and the Food and Drug Administration in sponsoring the National Research Council's Committee on Cancer Diagnosis and Therapy. Inasmuch as the work of this Committee will be described in detail by other witnesses, suffice it to say that it gives the nation a sound method of evaluating proposed cancer cures and diagnostic aids. It is the intention of our Association to encourage and further every honest attempt to increase our knowledge about cancer, to continue our earnest efforts in the quick dissemination of such knowledge to our physician members and to foster the type of cooperative research program previously outlined.

This concludes my formal statement. I want to thank the Committee for allowing our Association an opportunity to testify on this most important subject. I shall be happy to answer to the best of my ability any questions which members of the Committee may have.

NEW A. M. A. PUBLICATIONS

A revised catalog of medical and health films is now available. The Committee on Medical Motion Pictures has also published an index of all motion picture reviews published in THE JOURNAL from September, 1946, to December, 1952. Both booklets are available on request from the Committee on Medical Motion Pictures, American Medical Association, 535 North Dearborn Street, Chicago 10, Ill.

An attractive new pamphlet entitled "It's Your AMA" describes the many services that the American Medical Association performs for its members, for medical societies, and for the public. The brief illustrated pamphlet will be mailed to all A. M. A. members after Oct. 15 and in the future will be supplied to each new Association member. The pamphlet contains, for example, information on A. M. A. activities in the field of medical education, medical economics, evaluation of foods, drugs, cosmetics, and medical devices, legislation, health education, and postgraduate education. How the A. M. A. helps state and county medical societies by providing films, exhibits, recordings, and pamphlets, and information on any subject in the medical realm is described. Also stressed is the role of each individual physician in the work of the Association, pointing up the need for an active, informed membership, financial support, and loyalty.

JOINT MEETING ON RURAL HEALTH

Cooperation at the grass roots level between agricultural, medical, civic, and lay groups is necessary in order to obtain a still better understanding of rural health problems and to help solve them. This conclusion was reached during a recent joint meeting of the Advisory Committee, made up of members of various farm and agricultural organizations, and the Council on Rural Health. The chairman of the Council, Dr. F. S. Crockett, Lafayette, Ind., told the group: "The volume of rural health work in the country that has been done cannot be measured. We do not know the exact contributions that our Council has made, but we all feel that we have been traveling in the right direction. There have been phases that we have not emphasized sufficiently, but we have agreed that in the future each organization and this group collectively can do more in this activity to meet the needs of farm people. The major portion of our job is educational. It will require time and patience on the part of all groups involved. It only can be accomplished by cooperation at all levels, especially at the grass roots level."

The need for more physician participation at state and county levels was emphasized at the meeting. It was suggested that lay members talk with physicians to help interest them and that members of the Council devise ways and means through state and county medical societies of interesting physicians serving persons in rural areas. The importance of selecting members for the state and county rural health committees who have an understanding of and an interest in rural health was accentuated.

The advisory committee felt that national conferences have been most helpful in obtaining a further understanding of rural health needs but that there still is a problem of getting information to persons in rural areas. Advisory members were charged with the responsibility of making contacts within their associations to provide for closer cooperation between their groups and the members of the Council on Rural Health. It was suggested that county medical societies invite lay groups to meet with them in an effort to provide a better understanding of rural health problems.

The value of rural newspapers and farm journals as channels through which health information can reach more persons was emphasized at the meeting. More direct attention by the American Medical Association to informative news releases in lay language and the possibility of the regular distribution to rural newspapers and farm journals of lay-language articles on rural health problems by physicians were discussed. It was agreed that there is a need for greater understanding and use of prepaid medical and hospital insurance by rural populations. Each organization needs to develop a program to inform its membership of the availability and provisions of prepaid insurance. Directors of agricultural extension services and leaders of farm organizations can best be informed of organized medicine's interest in rural health problems, it was brought out, through organized medicine's participation in the meetings of these groups and through periodic contacts with these organizations.

Those who participated in the meeting were in accord that there was still a great need of the principles of "counciling together," although formal organization of "Health Councils" should be a secondary thought. It was suggested that a few interested groups get together informally to discuss rural health problems and, as the discussion groups progressed, additional organizations should be invited to join.

The advisory members present at the meeting were Mrs. Charles W. Sewell, Otterbein, Ind., member-at-large; Mrs. Charles DeShazo, Paul's Cross Roads, Va., Associated Women of the American Farm Bureau Federation; Mrs. J. Laning Taylor, Washington, D. C., National Milk Producers Federation; Miss Gertrude Humphreys, Morgantown, W. Va., agricultural extension services; Mr. Paul C. Johnson, Chicago, *Prairie Farmer* magazine; Mr. L. R. Neel, Nashville, Tenn., *Southern Agriculturist-Farm and Ranch* magazine; Mr. H. E. Slusher and Mr. Chester Starr, Jefferson City, Mo., Missouri Farm Bureau Federation; and Mr. Frank W. Peck, Chicago, the Farm Foundation.

THE OATH OF HIPPOCRATES

The Oath of Hippocrates is reproduced on this page in response to many requests.—ED.

I swear by Apollo, the physician, and Aesculapius, and Health, and All-heal, and all the gods and goddesses, that, according to my ability and judgment, I will keep this oath and stipulation: to reckon him who taught me this art equally dear to me as my parents, to share my substance with him and relieve his necessities if required; to regard his offspring as on the same footing with my own brothers, and to teach them this art if they should wish to learn it, without fee or stipulation, and that by precept, lecture and every other mode of instruction, I will impart a knowledge of the art to my own sons and to those of my teachers, and to disciples bound by a stipulation and oath, according to the law of medicine, but to none others.

I will follow that method of treatment which, according to my ability and judgment, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous. I will give no deadly medicine to anyone if asked, nor suggest any such counsel; furthermore, I will not give to a woman an instrument to produce abortion.

With purity and with holiness I will pass my life and practice my art. I will not cut a person who is suffering with a stone, but will leave this to be done by practitioners of this work. Into whatever houses I enter I will go into them for the benefit of the sick and will abstain from every voluntary art of mischief and corruption; and further from the seduction of females or males, bond or free.

Whatever, in connection with my professional practice, or not in connection with it, I may see or hear in the lives of men which ought not to be spoken abroad, I will not divulge, as reckoning that all such should be kept secret.

While I continue to keep this oath unviolated, may it be granted to me to enjoy life and the practice of the art, respected by all men at all times, but should I trespass and violate this oath, may the reverse be my lot.

ANNUAL CONFERENCE OF WOMAN'S AUXILIARY

The 10th annual conference of state presidents, presidents-elect, and national chairmen of the Woman's Auxiliary to the American Medical Association will be held at the Hotel LaSalle, Chicago, Nov. 18-20. The program comprises panel discussions on legislation, civil defense, organization, mental health, rural health, nurse recruitment, and the American Medical Education Foundation. The luncheon speakers will be Dr. Edward J. McCormick, President of the A. M. A., and Dr. Franklin D. Murphy, chancellor of the University of Kansas. The Friday program will be given at the A. M. A. headquarters, where several educational films will be presented. A tour of the headquarters building will follow luncheon there. Wednesday evening there will be a dutch treat dinner at the Edgewater Beach Hotel on the north side of the city.

DR. ELMER LEE HENDERSON

The following letter was recently received by Dr. Edward J. McCormick, President of the American Medical Association.

"The Board of Trustees, meeting at the 55th Annual Convention of the American Hospital Association in San Francisco, recognized the great loss to both the American Medical Association and the American Hospital Association in the death recently of that great leader in medical circles, Dr. Elmer Henderson.

"The Board of Trustees of the Association appreciated Dr. Henderson's efforts on behalf of hospitals. His passing is a great loss to all health agencies of this country."

MEDICAL NEWS

CALIFORNIA

Symposium on Immunity.—Stanford University School of Medicine, San Francisco, will present a symposium on immunity and hypersensitivity, Oct. 30-31, under the sponsorship of the M and R Laboratories, Columbus, Ohio. There will be no registration fee. All meetings will be held in Lane Hall, 2398 Sacramento St., in the Medical School Building.

General Practitioners Meet in Coronado.—The California Academy of General Practice will hold its annual scientific assembly at the Hotel del Coronado in Coronado, Oct. 25-27. Among the out-of-state speakers are Dr. Louis A. Buie, Rochester, Minn., Dr. Raymond W. McNealy, Chicago, Dr. Frederic H. Bentley, former professor of surgery, University of Durham, England, and now lecturer in surgery, Sommer Memorial Trust, Portland, Ore., and Alfred C. Kinsey, Sc.D., Bloomington, Ind. The meeting is open to all members of the academy and to any nonmember physician on payment of a $5 registration fee. Information may be obtained from the California Academy of General Practice, Suite 900, 461 Market St., San Francisco 5.

Symposium on Heart Disease.—The San Francisco Heart Association will hold its annual symposium on heart disease at the St. Francis Hotel, San Francisco, Oct. 28-30. Dr. David A. Rytand, San Francisco, will moderate an electrocardiographic pathological conference Wednesday, 9-10:30 a. m. The Wednesday afternoon session will open with a panel discussion, "Therapy of Rheumatic Diseases," at which Dr. Lowell A. Rantz, San Francisco, will serve as moderator. It will close with a panel discussion, "Cardiac Involvement in Noncardiac Pediatric Conditions," moderated by Dr. Henry D. Brainerd, San Francisco. Dr. Alfred F. Goggio, Berkeley, will be moderator for the panel discussion, "Present Status of Modern Cardiac Surgery," Thursday morning, and Dr. Robert L. Smith Jr., San Francisco, for the panel discussion "Chronic Coronary Disease" Thursday, 3:45-5 p. m. "Cardiac Drugs" is the title of the panel discussion Friday, 11:15 a. m., for which Dr. Eliaser will serve as moderator. Friday afternoon will be devoted to a clinical session in the Nurses' Auditorium, Mount Zion Hospital, with Dr. Arthur L. Bloomfield presiding. Guest speakers and their first presentations include:

Robert H. Bayley, Oklahoma City, Possible Clinical Applications of Vectorcardiography.
Howard B. Sprague, Boston, Uses and Limitations of Ballistocardiography.
Ann G. Kuttner, New York (participant in panel on rheumatic diseases).
Howard B. Burchell, Rochester, Minn., New Techniques in Diagnosis of Congenital Heart Disease with Particular Regard to Dye Dilution Curves.
Herrman L. Blumgart, Boston, Pathology and Clinical Classification of Cardiac Pain.
Robert L. King, Seattle, Greetings from the President of the American Heart Association.
Eugene A. Stead Jr., Durham, N. C., Present Views in Circulatory Failure.

COLORADO

Dr. Joslin to Deliver Harvard Lecture.—The sixth annual Harvard lecture will be delivered by Dr. Elliott P. Joslin, Boston, in the Sabin Auditorium, University of Colorado Medical Center, Denver, Oct. 30, 5 p. m. His lecture, "Diabetes, Today and Tomorrow," is given under the auspices of the Rocky Mountain Harvard Medical Alumni Association.

Course on Fractures and Joint Injuries.—The orthopedic division, University of Colorado School of Medicine, Denver, will present this course Nov. 19-21, with Dr. Edwin F. Cave, associate professor of orthopedics, Harvard Medical School, Boston, as guest lecturer. The course is designed to present to general practitioners the most practical methods of treatment of fractures and dislocations and other traumatic conditions. Sessions will be held at Colorado General Hospital, Denver General Hospital, Fitzsimons Army Hospital, and Childrens Hospital, all in Denver. For information, apply to the Office of Graduate and Postgraduate Medical Education, University of Colorado School of Medicine, 4200 E. Ninth Ave., Denver 20.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

DISTRICT OF COLUMBIA

Personal.—The Washington Heart Association has awarded its first clinical fellowship in cardiology to Dr. James J. Leonard.——The Ohio University Alumni Association has awarded a certificate of merit to Dr. James Alexander Lyon, Washington, D. C., "in recognition of distinguished attainments in the fields of internal medicine and cardiovascular diseases which reflect credit on his alma mater and are viewed with satisfaction by the Alumni Association."

University Receives Carrel Manuscript Collection.—The collection of manuscripts, comprising 60 cases of papers, amassed by the late Dr. Alexis Carrel has been donated to the Georgetown University Medical Center, Washington, D. C., by the surgeon's widow. Dr. Carrel, author of "Man, the Unknown," who collaborated with Charles A. Lindbergh on experiments in which tissues of a chicken heart were kept alive for several years in a mechanism constructed by the latter, was associated with the Rockefeller Institute for Medical Research from 1906 to 1939 and was member emeritus of the institute from 1939 until his death. Dr. Carrel was awarded the Nobel Prize in 1912 for his work in suturing blood vessels and the transplantation of organs.

ILLINOIS

Grants for Cerebral Palsy Research.—The United Cerebral Palsy Association has awarded three grants to the University of Illinois: (1) $19,313 for research in cerebral palsy with emphasis on disability evaluation and the application of physiological techniques for the facilitation of motor learning (under the direction of Dr. Frances A. Hellebrandt, department of physical medicine and rehabilitation); (2) $10,000 for investigation of the neuropharmacological aspects of cerebral palsy (conducted by Dr. Klaus R. Unna, department of pharmacology); and (3) $3,600 for a study of the treatment, designed to provide basic instruction in the clinical administration of cerebral palsy cases (under the direction of Beatrice D. Wade, O. T. R., department of occupational therapy).

Chicago

DeLee Lecture.—The Solomon Theron DeLee lecture, "Carbohydrates, Growth, and Pregnancy," will be given by Dr. Arthur St. George Huggett, professor of physiology, University of London, St. Mary's Hospital Medical School, at Chicago Lying-in Hospital, University of Chicago, 5841 Maryland Ave., Oct. 26, at 8:30 p. m.

Society News.—The Chicago Society of Industrial Medicine and Surgery will hold its fall scientific meeting at 8:30 p. m., Oct. 26, at the Palmer House (tel. RAndolph 6-7500). "The Emergency Care of Head Injuries" will be discussed by Dr. Harold C. Voris, clinical professor of surgery, neurosurgery division, Stritch School of Medicine of Loyola University. All persons of allied medical groups are cordially invited.

Dr. Snapper Returns to New York.—Dr. Isidore Snapper, director of medical education at Cook County Hospital and professor of medicine, Chicago Medical School, has been

appointed full time director of medical education by Beth-El Hospital, Brooklyn. Dr. Snapper came to Chicago about a year ago from New York, where he had served as clinical professor of medicine at Columbia University College of Physicians and Surgeons and as director of medical education at Mount Sinai Hospital.

Dr. Fulton to Deliver Ranson Lecture.—On Oct. 30, 4 p. m., Theta chapter of Phi Beta Pi, Northwestern University Medical School, will present the 24th annual Stephen Walter Ranson lectureship. Dr. John F. Fulton, Sterling Professor of the History of Medicine, Yale University School of Medicine, New Haven, Conn., will discuss "Contemporary Concepts of the Hypothalamus and Their Origin" at Thorne Hall, Superior St. and Lake Shore Dr. The lecture is open to physicians, students, and other interested persons.

KANSAS

Dr. William Menninger Honored.—The Alumni Association of Cornell University Medical College recently bestowed the award of distinction on Dr. William C. Menninger, Topeka, professor of psychiatry, University of Kansas School of Medicine, Kansas City, and general secretary, the Menninger Foundation, "in recognition of his notable achievements in the teaching and practice of psychiatry, whose life and work have brought honor and acclaim to his medical college." Dr. Menninger in World War II was director of the neuropsychiatry consultants' division, Surgeon General's Office. He received the Distinguished Service medal and Army Commendation ribbon, and is a Chevalier of the French Legion of Honor.

Course on Orthopedics and Physical Medicine.—Physical medicine in its practical application to orthopedic practice will be presented in the refresher course, "Orthopedics, Physical Medicine, and Rehabilitation," Oct. 26-28, at the University of Kansas Medical Center, Kansas City. The course is a part of the postgraduate medical study sponsored by the University of Kansas in cooperation with the Kansas Medical Society and the Kansas State Board of Health. Round-table discussions by guest instructors and the staff will be held at the close of each day's program: Monday, "Fractures"; Tuesday, "Amputation and Prostheses," "Backache"; and Wednesday, "Arthritis." Guest instructors include Drs. Alexander P. Aitken, Boston; James L. Beaver, Wichita; Walter P. Blount, Milwaukee; Miland E. Knapp, Minneapolis; Jesse T. Nicholson, Philadelphia; and William D. Paul, Iowa City.

LOUISIANA

University News.—At Tulane University of Louisiana School of Medicine, New Orleans, members of the freshman class recently presented a portrait of Harold Cummins, Ph.D., assistant dean and professor of anatomy, to the university. Members of the staff of the department of obstetrics and gynecology, both past and present, gave a portrait of their chief, Dr. Conrad G. Collins.——When the Nebraska State Medical Society held its "Tulane University Day," Dr. Isadore Dyer, professor of obstetrics, Tulane University of Louisiana School of Medicine, New Orleans, spoke on "Obstetric Aspects of Prematurity—Prevention and Management," Dr. Conrad G. Collins, professor of gynecology on "Ectopic Pregnancy," and Dr. H. Reichard Kahle, associate professor of surgery, on "Intussusception: Diagnostic and Therapeutic Considerations."

Personal.—Dr. Leon J. Menville, emeritus professor of radiology, Tulane University of Louisiana School of Medicine, New Orleans, was recently made an honorary member by the Radiological Society of North America. During the 38 years of its existence, the society has conferred this honor on only eight persons.——Dr. William A. Sodeman, professor of preventive tropical and semitropical diseases and hygiene, Tulane University of Louisiana School of Medicine, has been appointed chairman of the department of medicine at the University of Missouri School of Medicine, Columbia.——Dr. Harold J. Jacobs, formerly clinical instructor of internal medicine, Louisiana State University School of Medicine, New Orleans, has been appointed director of the cardiac and pulmonary laboratories and also director of medical education at De Paul Hospital, Norfolk, Va.

MAINE

Venereal Disease Clinics.—The state department of health and welfare, bureau of health, maintains facilities for the diagnosis and treatment of venereal diseases in the following locations: Augusta, Bangor, Bath, Belfast, Biddeford, Lewiston, Portland, Rockland, Rumford, Sanford, Waterville, Wilton, and Winthrop. Any physician wishing to refer an indigent person for diagnosis or treatment may obtain the name of the nearest clinic physician by contacting the department at the state house in Augusta. If no clinic facilities are available, physicians will be authorized to treat indigent patients in their offices. Authorization should be requested before treatment is started.

Clinical Session of State Association.—The fall clinical session of the Maine Medical Association will have its headquarters at Bangor House, 174 Main St., Oct. 25-26. Sunday, 6:30 p. m., Dr. Sara M. Jordan, chief of the gastroenterology section, Lahey Clinic, Boston, will address the dinner meeting for physicians and wives. Her subject will be "Digestion, Diet, and Doctors." The clinical program will be presented Monday at the Eastern Maine General Hospital, Bangor. Dr. Jordan will serve as guest moderator for the morning program, which includes orthopedic cases, gastric bleeding, intestinal polyps, regional ileitis, and fluid and electrolytes in surgery. Dr. Edward B. D. Neuhauser, roentgenologist, Infants' Hospital, Boston, will comment on the afternoon topics: selection of cases for cardiac surgery, infantile cortical hyperostosis, selected orthopedic cases from children and young adults, and mediastinal tumors. Dr. Neuhauser will discuss "Pediatric Roentgenology in General Practice" at the dinner Monday, 6:30 p. m.

MASSACHUSETTS

Personal.— The fourth annual Joseph L. Baer lecture, "Carcinoma in Situ of Cervix: Further Studies on Its Relationship to Cervical Carcinoma," was delivered before the Chicago Gynecological Society, Oct. 16, by Dr. Arthur T. Hertig, head of the department of pathology, Harvard Medical School, Boston.

New England Center Lectures.—The House Officers' Association, New England Center Hospital, is holding an evening lecture series. On Oct. 28, 7 p. m., Dr. Graham M. Bull, professor of medicine, Queen's University of Belfast, Belfast, North Ireland, will present "Postural Proteinuria" in the Stearns Auditorium, New England Center Hospital, Harrison Ave. and Bennet St., Boston. Discussors will be Drs. Alexander Leaf and Joseph M. Hayman Jr., Boston.

MICHIGAN

Beaumont Memorial.—The cornerstone for the Beaumont Memorial on the site in Mackinac Island where the Michigan State Medical Society is restoring the trading store of the American Fur Company, was laid on July 17 (see THE JOURNAL, May 3, 1952, p. 70; March 28, 1953, p. 117). Dr. Reader J. Hubbell, Kalamazoo, president, Michigan State Medical Society, the Hon. W. F. Doyle, Mackinac Island State Park Commission, and Dr. Otto O. Beck, Birmingham, chairman, Beaumont Memorial Fund, officiated at the cornerstone laying. Participating in the ceremony were Dr. William S. Jones, Menominee; Dr. Albert H. Miller, Gladstone; Dr. William Bromme, Detroit; Dr. Alfred H. Whittaker, Detroit; the Hon. G. Mennen Williams, governor of Michigan; the Hon. Leslie O'Brien, mayor of Mackinac Island; and the Rev. Thomas W. Murphy, Detroit. The ceremony commemorated the historical episode on June 19, 1822, when Dr. William Beaumont began the treatment of Alexis St. Martin for a gaping gunshot wound in the stomach and, through his observations on the gastric fistula became the first to study the process of digestion in life.

MINNESOTA

Dr. Vadheim Appreciation Day.—Dr. Alfred L. Vadheim, Tyler, was honored by his community, which celebrated "Vadheim Appreciation Day" to mark the 43rd anniversary of his arrival in Tyler. Dr. Vadheim has served as mayor and as a member of the school board, has been active in Boy Scout work, and assisted in establishing the library. As Red Cross director for Lincoln County, he brought the county national honor in 1941 when it became the first in the world to become accredited for the control of tuberculosis.

Rigler Lecture.—The annual Leo G. Rigler lecture will be presented at the University of Minnesota, Minneapolis, Oct. 28, by Dr. Robert McWhirter, professor, department of radiotherapy, Royal Infirmary, Edinburgh. His subject will be "Simple Mastectomy and Postoperative Irradiation for Carcinoma of the Breast." Dr. McWhirter will also participate in the continuation course in radiation therapy which will be presented by the university, Oct. 25-31, under the direction of Dr. Leo G. Rigler and Karl W. Stenstrom, Ph.D.

MISSOURI

Society News.—The St. Louis Pediatric Society has elected Dr. Harry E. Wachter, president; Dr. Raymond J. LaDriere, vice-president; and Dr. Leo F. Gowen, secretary-treasurer. Meetings are held at Medart's Restaurant on the second Thursday of each month from October through May.——At the annual meeting of the St. Louis Ophthalmological Society, the following officers were elected: president, Dr. Harry D. Rosenbaum; vice-president, Dr. James H. Bryan; treasurer, Dr. Ruth S. Freedman; secretary, Dr. Anton J. Hummel; and member-at-large, Dr. Robert D. Mattis.

General Practitioners Meet in Jefferson City.—The Missouri Academy of General Practice will hold its annual scientific assembly at the Governor Hotel, Jefferson City, Oct. 28-29. At the Wednesday luncheon session, Dr. Ralph A. Kinsella, St. Louis, will present "Evaluation of Chest Pain." Other speakers on the Wednesday afternoon program include Drs. Henry R. McCarroll and Joseph C. Jaudon, St. Louis; Thomas E. McMillan, Kansas City; and Paul S. Williamson, Walsh, Colo. Dr. Roscoe L. Pullen, dean, University of Missouri School of Medicine, Columbia, will be guest speaker at the annual banquet Wednesday evening. Essayists on the Thursday program (Drs. Charles A. Brasher, Mount Vernon; Harry B. Stauffer, Jefferson City; Carl A. Moyer, St. Louis; William A. Sodeman, Columbia; and Paul S. Williamson, Walsh, Colo.) will also take part in a luncheon round-table discussion Thursday noon.

NEBRASKA

Dr. Kriz Presents Pool to Home Town.—Dr. Rudolph E. Kriz recently presented a $14,000 swimming pool to the city of Lynch whose citizens assisted in construction of the pool by furnishing labor and equipment for the excavating.

NEW HAMPSHIRE

Society News.—The New Hampshire Society of Anesthesiologists has elected the following officers for 1953: president, Dr. Frank G. Dudley, Littleton; vice-president, Dr. Angus M. Brooks, Concord; and secretary-treasurer, Dr. Agnes V. Bartlett, Springfield, Vt.

NEW JERSEY

Clinic for Amputee Children.—The Kessler Institute for Rehabilitation, Pleasant Valley Way, West Orange, will hold a free clinic for congenital amputee children and their parents Oct. 24.

Award to Dr. Orton.—The Academy of Medicine of Northern New Jersey presented its Edward J. Ill Award, to Dr. Henry B. Orton, professor of laryngeal surgery, New York Polyclinic Medical School and Hospital, New York. Dr. Orton is credited with having made important contributions in cancer of the larynx and, in his fight to prevent injuries to children from lye-containing household products, with having been instrumental in passage of a law by the state legislature of New Jersey, which requires that every product containing lye be marked poison.

Society News.—The New Jersey Allergy Society has elected the following officers for the coming year: president, Dr. Edward E. Seidmon, Plainfield; vice-president, Dr. William B. Nevius, East Orange; treasurer, Dr. Eugene J. Luippold, Boonton; and secretary, Dr. Frank Rosen, Newark.——At the annual meeting of the New Jersey Society of Clinical Pathologists, the following officers were elected for 1953-1954: president, Dr. Thomas K. Rathmell, Trenton; vice-president, Dr. George L. Erdman, Summit; and secretary-treasurer, Dr. Robert Brill, Passaic.——An award for "outstanding services to the society" was made to Elmer L. Shaffer, Ph.D., director of laboratories, New Jersey State Health Department. The program for the year includes tissue seminars, seminars in clinical pathology, and a special seminar in cooperation with the State Society of Medical Technologists.

NEW YORK

Hospital News.—The Mount Sinai Hospital, New York, announces that the weekly clinical pathological conferences by Dr. Paul Klemperer and Dr. Alexander B. Gutman and staff will be resumed Oct. 28, 3:30 p. m., and that weekly medical grand rounds by Dr. Gutman and staff will be resumed Oct. 30, 3 p. m., in the Blumenthal Auditorium of the Mount Sinai Hospital (entrance on Fifth Ave. at 99th St. through the hospital gardens).

Cardiac Teaching Day.—A postgraduate teaching day on heart disease for physicians and medical students will be held Oct. 29 at the Rochester Academy of Medicine, 1441 East Ave. At 2 p. m. Dr. Richard H. Lyons, Syracuse, will discuss "Treatment of Intractable Cardiac Failure," and at 3 p. m. Dr. Paul M. Zoll, Boston, will present "Recent Advances in Knowledge of Coronary Circulation." There will be a clinical pathological conference at 4 p. m.

Lecture on Chronic Arthritis.—At a meeting of the combined staffs of Binghamton City Hospital, Oct. 26, 8 p. m., at the hospital, Dr. Russell L. Cecil, professor of clinical medicine, Cornell University Medical College, New York, will discuss "The Treatment of Chronic Arthritis." This program of postgraduate instruction is arranged by the state council committee on public health and education, Medical Society of the State of New York, in cooperation with the New York State Department of Health.

Meeting of General Practitioners.—The annual scientific session of the New York State Academy of General Practice will convene at the Hotel Statler, New York City, Oct. 26-28. Each day's program will terminate with a round-table discussion at 3:15 p. m. by the speakers of the day: Monday, pediatric problems: Dr. Philip M. Stimson, New York City (poliomyelitis); Dr. John R. Cobb, New York City (orthopedic problems); Dorothy W. Baruch, Ph.D., Beverly Hills, Calif. (juvenile delinquency); and Dr. Samuel Karelitz, New York City (contagious diseases). Tuesday, adult problems: Dr. Walter C. Alvarez, Chicago (our neurotic population); Dr. Philip Thorek, Chicago (acute surgical emergencies in adults); Dr. Harold A. Abramson, New York City (psychosomatic allergy); Dr. Louis M. Hellman, Brooklyn (gynecologic problems); and Alfred C. Kinsey, Sc.D., Bloomington, Ind. (sexual behavior in the adult). Wednesday, geriatric problems: Dr. Edward J. Stieglitz, Washington, D. C. (patients, 70 years and older); Dr. Howard A. Rusk, New York City (rehabilitation of the aged); Dr. Alvarez (geriatric neuroses); Dr. Nolan D. C. Lewis, New York City (geriatric psychosis); and Dr. Louis H. Bauer, Hempstead (socioeconomic problems of the aged). Dr. Rusk and staff will hold a clinic at the Rehabilitation Center, Thursday at 10 a. m.

New York City

Hospital News.—The division of neoplastic diseases, Montefiore Hospital for Chronic Diseases, is presenting a series of conferences at 3 p. m. on the first Friday of each month in the social hall. On Nov. 6 "Endocrine Approaches to the Cancer Problem" will be the topic of Dr. Roy Hertz, chief, research medicine branch, National Cancer Institute, Bethesda, Md.

Lecture on Oral Pathology.—Lester R. Cahn, D.D.S., associate professor, oral pathology, Columbia University School of Dental and Oral Surgery of the Faculty of Medicine, will give a lecture, "The Practical Application of Basic Pathology: Inflammation and Repair," at the conference of the New York Institute of Clinical Oral Pathology, 9 p. m., Oct. 26, at the New York Academy of Medicine, room 440.

Cofer Memorial Chapel.—The Leland Eggleston Cofer Memorial Chapel, adjacent to the main entrance lobby of the New York Hospital, was recently dedicated as a nondenominational chapel in memory of Dr. Leland Eggleston Cofer, who died in 1948 after a distinguished career in surgery and public health, including such posts as commissioner of health of the Hawaiian Islands and commissioner of the port of New York. Mr. Hamilton Hadley, vice-president of the Society of the New York Hospital, thanked Mrs. Cofer and an anonymous donor for their gifts, which "have given us what we have not had in all our 182 years of history . . . a chapel."

Personal.—Dr. James Marion Bryant, who is in charge of inpatient cardiology on the fourth medical division of New York City's Bellevue Hospital, under the direction of Dr. Charles F. Wilkinson Jr., professor of medicine for the Post-Graduate Medical School of New York University-Bellevue Medical Center, has been appointed assistant professor of medicine at the school.——The Department of Defense, Washington, D. C., recently awarded a certificate of appreciation to Dr. Julius Lempert, surgical director of the Lempert Institute of Otology, who for several years has voluntarily accepted in his graduate classes specialists in otolaryngology from the Armed Forces Medical Services.

Course on Surgery of the Hand.—The New York and Brooklyn Regional Committee on Trauma of the American College of Surgeons announces a course on surgery of the hand, Dec. 11-12, 9 a. m. to 5 p. m. The course will be given at the Lenox Hill Hospital Einhorn Auditorium, 76th St. and Lexington Ave., by Drs. Joseph H. Boyes, Los Angeles; John H. Couch, Toronto, Canada; Michael L. Mason, Chicago; and J. William Littler, Robert H. Kennedy, Harrison L. McLaughlin, Ernest W. Lampe, and Thomas W. Stevenson Jr., all of New York. Advance registration is necessary. Communicate with Dr. Frederick M. Smith, Secretary, 180 Fort Washington Ave., New York 32.

NORTH CAROLINA

Lectures on Obstetrics.—A series of lectures on obstetrics has been arranged as part of a postgraduate medical course at Morganton, sponsored by the University of North Carolina School of Medicine, Chapel Hill, and the extension division, with the cooperation of a committee of physicians from Burke and adjoining counties. On Oct. 28 Dr. Edward A. Schumann, Philadelphia, will present "Toxemias of Pregnancy" at 4 p. m. and will discuss "Problems of Fetal and Neonatal Mortality" at 7:30 p. m.

NORTH DAKOTA

Meeting on Public Health.—The North Dakota Public Health Association will have its annual meeting at the Ray Hotel in Dickinson, Oct. 26-27. Featured speakers will include the Hon. C. Norman Brunsdale, governor of North Dakota; Dr. Charles F. Blankenship, regional medical director, U. S. Public Health Service, Kansas City, Mo.; and Dr. Russell O. Saxvik, state health officer, state department of health, Bismarck.

OHIO

Society News.—The sixth councilor district, Ohio State Medical Association, will hold its annual postgraduate day Oct. 28 at the St. Francis Hotel, Canton. Panel discussion topics include (1) "Infectious Diseases of the Pancreas and Chronic Relapsing Pancreatitis" and (2) "Chronic Ulcerative Colitis and Regional Enteritis." Among the panel members will be Drs. Robert M. Zollinger, Ohio State University College of Medicine, Columbus, moderator; Sara M. Jordan and Kenneth W. Warren, Lahey Clinic, Boston; Philip F. Partington, Western Reserve University School of Medicine, Cleveland; Everett N. Collins, and J. Beach Hazard, Cleveland Clinic. Papers will be presented by Drs. Jordan, Hazard, Partington, and Dr. Warren. Dr. Richard H. Overholt, Tufts College Medical School, Boston, will speak during the evening program on the subject, "The Fourth Dimension in Thoracic Surgery." Reservations may be made through Mr. E. M. Sprunger, executive secretary, Stark County Medical Society, 400 Fourth St., N. W., Canton 2.

OKLAHOMA

Meeting of Anesthesiologists.—Dr. Douglas W. Eastwood, St. Louis, will be guest speaker at the annual fall meeting of the Oklahoma Society of Anesthesiologists, Oct. 25, at the Oklahoma Club in Oklahoma City.

PENNSYLVANIA

Society News.—The Heart Association of Southeastern Pennsylvania is holding classes in dietary instruction for cardiovascular patients from the Philadelphia area in the Sheppard building of Woman's Hospital, Parrish and Preston Sts., on the first Tuesday of each month from 7 to 8 p. m. Any patient, private or clinic, whose physician believes he would benefit by professional guidance in following a reducing, salt free, or other type of special diet, is eligible to attend these classes. This free service is provided by the division of adult cardiovascular diseases of the Department of Health of the Commonwealth of Pennsylvania. Appointments may be made by contacting the Heart Association of Southeastern Pennsylvania, 1505 Walnut St., telephone LO 4-1185.

Philadelphia

Society News.—The annual meeting of the Philadelphia Allergy Society will be held Oct. 28 at the College of Physicians. Dr. Oscar Swineford Jr., Charlottesville, Va., will speak on "Background Observations on the Bacterial Allergy Problem." In a panel discussion, which will follow, Dr. Swineford will talk on "Asthma," Dr. Harry P. Schenck on "Allergic Rhinitis," and Joseph Smolens, B.S., on "Bacterial Antigens." Papers on allergy will be presented by Drs. David Myers and Alexander Sterling.

Pemberton Memorial Lecture.—The Philadelphia County Medical Society announces that the Ralph Pemberton Memorial lecture will be presented by Dr. Charles A. Ragan Jr., associate professor of medicine, Columbia University College of Physicians and Surgeons, New York, Oct. 29 at 9 p. m. His subject will be "The Pathologic Physiology of Bone and Joint Disease." The society will hold an afternoon program on therapy of the rheumatic diseases, beginning at 2 p. m. and terminating with a panel discussion at 4 p. m. Cocktails, 6:30 p. m., will precede a subscription dinner open to the medical profession.

SOUTH CAROLINA

Personal.—Dr. William S. Fewell has retired from general practice and will serve as full-time medical director of the Liberty Life Insurance Company, Greenville, S. C.

Society News.—At a recent meeting of the South Carolina Society of Anesthesiologists the following officers were elected: president, Dr. John M. Brown, Charleston; vice-president, Dr. Richard Wayburn, Columbia; and secretary-treasurer, Dr. George L. Timmons, Hartsville.

TEXAS

Hospital News.—The University of Texas Medical Branch in Galveston announces that completion of the new John Sealy Hospital building and of the Henry and Rosa Ziegler Memorial Hospital for diseases of the chest will increase the bed capacity of the medical branch hospitals from 700 to 1500. Opportunities are being offered for intern training in hospital administration under the direction of Mr. Edgar N. Appleman, C.P.A., recently appointed acting administrator of the University of Texas Medical Branch Hospitals in Galveston.

VERMONT

Research Grants.—The National Institute of Health has awarded research grants totaling $46,920 to the following members of the faculty of the University of Vermont College of Medicine, Burlington: Dr. Eugene Lepeschkin, associate professor of experimental medicine, $15,380; Dr. Ethan A. Sims, assistant professor of medicine and biochemistry, and Dr. Kermit E. Krantz, assistant professor of obstetrics and gynecology, $12,181 for a study of renal function in pregnant women; Dr. Oscar S. Peterson, associate professor of radiology, $14,931 (continuing grant) for the development of rotational x-ray therapy, and Arnold H. Schein, Ph.D., associate professor of biochemistry, $4,428 for study of a chemical problem under the title "Purification of the Purine Oxidizing Enzymes, Xanthine Oxidase, Uricase, and Guanase."

Symposium on Cardiovascular Diseases.—At the annual meeting of the Vermont Heart Association, Oct. 26-30, in the Fleming Museum, Burlington, a symposium on cardiovascular diseases will be held in cooperation with the Vermont Heart Commission and the University of Vermont College of Medicine, Burlington. Monday, 9:30 a. m., Dr. Louis A. Selverstone, Boston, will present "Symptoms and Signs of Cardiovascular Disease" and at 2 p. m. will speak on congestive cardiac failure. At 4 p. m. there will be a case presentation on congestive cardiac failure at Bishop DeGoesbriand Hospital. Tuesday, 9:30 a. m., Dr. James H. Currens, Boston, will talk on electrocardiograms, and at 2 p. m. Dr. Gordon S. Myers, Boston, will discuss "Diagnosis and Management of Cardiac Arrhythmias." Case presentations on arrhythmias will be made at the Mary Fletcher Hospital, Durfee Clinic, 4 p. m. Wednesday morning Dr. James A. Evans, Boston, will discuss the diagnosis and medical management of hypertension, and in the afternoon Dr. Edwin F. Lang, Boston, will speak on surgical management, selection, and operative procedures in hypertension. Case presentations in hypertension will be made at the Durfee Clinic at 4 p. m. Thursday morning will be devoted to a paper, entitled "Pitfalls in the Diagnosis and Treatment of Cardiac Emergencies," by Dr. Conger Williams, Boston, and Thursday afternoon to a panel discussion on problems of the cardiac, for which Dr. George A. Wolf Jr., Burlington, will serve as moderator. The annual meeting of the Vermont Heart Association will be held at 4 p. m. Discussion of coronary disease by Dr. E. Hugh Luckey, New York, 9:30 a. m. Friday, will be followed by case presentations on coronary disease. Friday afternoon "The Rheumatic Fever Program" will be presented by Drs. Robert J. McKay and Olive M. Davies, Burlington, and "The Cardiopulmonary Diagnostic Clinic" by Dr. Donald B. Miller, Burlington. Formal opening of the Cardiopulmonary Clinic and a tour of inspection are scheduled at the Mary Fletcher Hospital at 3 p. m.

WASHINGTON

Meeting of General Practitioners.—The Washington chapter of the American Academy of General Practice will hold its annual convention and scientific session in the Chinook Hotel in Yakima, Oct. 30-31. Among the speakers will be Dr. Raymond W. McNealy, Chicago; Dr. Peter H. Forsham, San Francisco; and Mac F. Cahal, executive secretary of the American Academy of General Practice, Kansas City, Mo.

Fifty Year Buttons.—During its annual convention in Seattle the Washington State Medical Association awarded gold lapel buttons in recognition of 50 years of medical practice to Drs. Richard W. Perry, Fordyce C. Gorham, Clyde A. Fitzgerald, Francis M. Carroll, Herbert H. Canfield, David H. Houston, John E. Godfrey, Frank T. Maxson, Walter J. Howells, Park Weed Willis Sr., Maimon Samuels, and Lilian C. Irwin, all of Seattle; Leon L. Goodnow and Oliver R. Austin, Aberdeen; Herbert L. Underwood, Vancouver; Joseph E. Midgett, Des Moines; John P. Schutt, Bremerton; Arthur B. Cook, Anacortes; William A. Mitchell, Colfax; Charles E. Conway, Cashmere; Clyde E. Gray, Tacoma; Orme R. Nevitt, Raymond; and Harry E. Rhodehamel, Spokane.

WISCONSIN

Personal.—The following new members of the Wisconsin State Board of Medical Examiners have been named by Gov. Walter J. Kohler: Drs. John A. Schindler, Monroe, and Millard Tufts, Milwaukee, to replace Drs. Anthony F. Rufflo, Kenosha, and Ernest W. Miller, Milwaukee, whose terms ended July 1; Drs. Jerry W. McRoberts, Sheboygan, Thomas W. Tormey Jr., Madison, and Clifford A. Olson, Baldwin, to replace Drs. John W. Smith, Milwaukee, and Henry H. Christofferson, Colby, who resigned their positions, and to fill the position left vacant in 1951 by the death of Dr. Charles A. Dawson, River Falls.

University News.—The following promotions are announced by the University of Wisconsin Medical School, Madison: Dr. Ann Bardeen from instructor to assistant professor of anesthesia; in the department of medicine, Drs. Edgar S. Gordon and Marc J. Musser from associate professor to professor; Dr. Thomas H. Lorenz from instructor to assistant professor; Dr. John LeRoy Sims from assistant professor to associate professor; and Dr. H. Kent Tenney from associate professor to clinical professor (pediatrics); in the department of surgery (ophthalmology), Dr. Peter A. Duehr from associate professor to clinical professor of ophthalmology; Drs. John V. Berger and Frederick J. Davis from instructor to assistant clinical professor of ophthalmology; and Dr. Eleanor Maxine Bennett from instructor to associate professor.

Cancer Teaching Clinics.—Cancer diagnostic teaching clinics will be held at the Lutheran Hospital, Eau Claire, Oct. 27; the Memorial Hospital, Wausau, Oct. 28; and St. Elizabeth's Hospital, Appleton, Oct. 29. The following program will be presented, 2-5:15 p. m.:

Uterine Cancer, Roy G. Holly, Minneapolis.
Lung Cancer, Hiram T. Langston, Chicago.
Cytologic Diagnosis of Cancer, Gordon Worley Jr., Madison.
Oral Cancer, Frank D. Bernard, Madison.

At 6:30 p. m. there will be a dinner meeting with dentists (Eau Claire, Hotel Eau Claire; Wausau, Wausau Club; and Appleton, The Elks Club). Dr. Frank D. Bernard will present "The Dentist and the Physician—A Team in the Diagnosis of Early Oral Malignancies." Through funds made available by the American Cancer Society, Wisconsin division, these clinics are open to members of the State Medical Society of Wisconsin and Wisconsin State Dental Society without charge. Reservations are necessary for the dinner ($3). Requests should be sent to Dr. Anthony R. Curreri, Chairman, Committee on Cancer, SMS, 704 E. Gorham St., Madison.

GENERAL

Society News.—The annual meeting of the **American Academy for Cerebral Palsy** will be held Oct. 30-31 at the Western Hills Hotel, Ft. Worth, Texas. The scientific sessions are open to members of the medical or allied professions.

Meeting on Clinical Research.—The Central Society for Clinical Research will meet at the Drake Hotel, Chicago, Oct. 30-31. Dr. George E. Burch Jr., New Orleans, will deliver the presidential address during the Friday morning session. Participants in the 35 presentations that have been scheduled will include 49 speakers by invitation.

Meeting of Medical Colleges.—The Association of American Medical Colleges will hold its annual meeting at the Claridge Hotel, Atlantic City, N. J., Oct. 26-28, under the presidency of Dr. Ward Darley, Denver. The chief findings and recommendations of the survey of premedical education will be presented Tuesday at 10 a. m. by Aura E. Severinghaus, Ph.D., Columbia University College of Physicians and Surgeons, New York, and the chief findings and recommendations of the survey of medical education, at 2 p. m. by Dr. John E. Deitrick, Jefferson Medical College, Philadelphia. At 9 p. m. there will be a film program, medical audio-visual institute.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories, and possessions in the weeks ended as indicated:

Area	Oct. 10, 1953 Paralytic Type	Oct. 10, 1953 Total Cases Reported	Oct. 11, 1952 Total
New England States			
Maine	7	20	7
New Hampshire	..	..	3
Vermont	1	7	3
Massachusetts	15	36	33
Rhode Island	..	14	10
Connecticut	5	12	18
Middle Atlantic States			
New York	36	131	139
New Jersey	20	45	36
Pennsylvania	..	76	82
East North Central States			
Ohio	20	126	190
Indiana	..	15	155
Illinois	19	48	280
Michigan	34	89	252
Wisconsin	..	46	104
West North Central States			
Minnesota	15	74	302
Iowa	7	21	158
Missouri	5	18	75
North Dakota	2	6	9
South Dakota	..	4	79
Nebraska	2	6	99
Kansas	4	15	81
South Atlantic States			
Delaware	1	1	4
Maryland	18	26	10
District of Columbia	..	1	4
Virginia	8	15	34
West Virginia	7	19	16
North Carolina	6	10	34
South Carolina	1	5	10
Georgia	4	8	31
Florida	18	46	32
East South Central States			
Kentucky	4	7	60
Tennessee	7	11	22
Alabama	5	8	6
Mississippi	..	2	19
West South Central States			
Arkansas	6	9	15
Louisiana	11	19	13
Oklahoma	..	12	39
Texas	11	22	43
Mountain States			
Montana	7	12	17
Idaho	..	3	10
Wyoming	1	4	11
Colorado	4	4	46
New Mexico	..	2	14
Arizona	6	13	26
Utah	..	1	13
Nevada	3	3	4
Pacific States			
Washington	..	20	50
Oregon	8	12	34
California	80	186	138
Territories and Possessions			
Alaska	..	..	7
Hawaii	..	..	2
Puerto Rico	..	..	4
Total	417	1,290	2,883

Southwestern Medical Association.—The annual meeting of the Southwestern Medical Association is scheduled to be held at the Pioneer Hotel, Tucson, Ariz., Oct. 29-31. Presentations by guest speakers include:

William P. Thompson, Los Angeles, (1) Selection of Patients for Mitral Commissurotomy. (2) Prevention of Coronary Thrombosis. (3) Management of Congestive Heart Failure.

Donovan C. Browne, New Orleans, (1) Controversial Problems in Management of Peptic Ulcer. (2) Postgastrectomy Dumping Syndrome. (3) Management of Chronic Ulcerative Colitis.

Henry K. Ransom, Ann Arbor, Mich., (1) Diverticulitis of the Colon. (2) Surgical Treatment of Duodenal Ulcer. (3) Diseases of the Breast.

Drs. Edmund B. Spaeth, Philadelphia, Merl J. Carson, Los Angeles, and Marion B. Sulzberger, New York, will also participate in the program (subjects to be announced).

Meeting on Mental Health.—The National Association for Mental Health will hold its annual meeting at the Hotel Carter, Cleveland, Oct. 31 to Nov. 2. The theme of the conference, "Mental Health—Everybody's Business," will be introduced with presentation of "Everyone Has a Stake in Community Mental Health," by Dr. George S. Stevenson, national and international consultant of the association, which will be followed by a panel discussion at 10 a. m. At 12:30 p. m. Dr. Erich Lindemann, Boston, will discuss "Preventive Psychiatry for the Total Community" at the keynote luncheon in the Rainbow Room. Workshops on activities of mental health associations will be conducted at 2:30 p. m. On Sunday, 2:30 p. m. in the grand ballroom there will be a panel discussion, "Toward Greater Citizen Participation." At 8 p. m. in the grand ballroom there will be an open discussion on education in mental health. This will include idea exchange of educational activities used by state and local mental health associations in informing the public about mental health. Monday, 9 a. m., in the grand ballroom, a program on progress in improved care of the mentally ill will be presented. At 10:30 a. m. Dr. Walter H. Baer, Peoria, Ill., will be discussion leader for workshops on activities of mental health associations related to psychiatric aids. Dr. Paul Lemkau, Baltimore, will preside at luncheon in the Petit Cafe 12:30 p. m., at which the speakers will be Dr. William Malamud, Boston, director, NAMH research in dementia praecox, and Mr. Raymond G. Fuller, New York, director, study of administration of state psychiatric services. At 2:30 p. m. in the grand ballroom, Luther Woodward, Ph.D., director, community services, New York State Mental Health Commission, will have as his topic, "Rehabilitation of the Mentally Ill."

Southern Medical Association.—The 47th annual meeting of this association will be held at the Municipal Auditorium, Atlanta, Oct. 26-29. The opening assembly will be a public session Monday, 10:30 a. m., at which Dr. Walter C. Jones, Miami, Fla., president, will deliver an address, "Forgive Us Our Debts." His presentation will be followed by a discussion, entitled "Federal Medicine, Its Impact on the Medical Care of the American People," by Dr. Walter B. Martin, Norfolk, Va., President-Elect of the American Medical Association. On Tuesday the Hon. James C. Davis, representing the Fifth Congressional District of Georgia, will address the section on general practice at a luncheon meeting in the Dinkler Plaza Hotel, Civic Room, at noon. His subject will be "Socialized Medicine and Free Enterprise." The section on medicine will have a panel discussion Tuesday on newer techniques and problems in medical diagnosis and Thursday on the use of newer therapeutic agents. A panel on amebiasis will be presented by the section on gastroenterology Tuesday afternoon, and Wednesday morning the Southern Electroencephalographic Society will have a panel discussion on technique, instrumentation, procedures and problems in clinical electroencephalography. "Anesthesia in Urology" is the topic for the panel discussion to be presented Wednesday, 9 a. m., by the section on anesthesiology. The section on allergy has planned a round-table discussion on pediatric atopic dermatitis (eczema) for Tuesday afternoon. Wednesday afternoon "Research in the Clinical Center of the National Institutes of Health, Public Health Service," will be explained by Dr. William H. Sebrell Jr., Bethesda, Md., who will illustrate his

talk with lantern slides. Motion pictures will be shown in the Municipal Auditorium, Tuesday and Wednesday, 9 a. m. to 5:30 p. m. The association dinner and dance will be held at the Atlanta Biltmore Hotel, Wednesday, 7 p. m.

CANADA

Lecture on Thyroid Disease.—The 16th annual Louis Gross Memorial lecture, under the auspices of the Montreal Clinical Society, will be delivered at the Jewish General Hospital, Montreal, Quebec, Oct. 29, 8:30 p. m. by Dr. Martin M. Hoffman, associate professor of medicine and psychiatry, McGill University Faculty of Medicine, Montreal. The subject will be "The Physiopathology of Thyroid Disease."

LATIN AMERICA

Venezuelan Health Director to WHO Staff.—Dr. Carlos Luis Gonzalez, director of public health of Venezuela, has been appointed chief of the division of public health, Pan American Sanitary Bureau, Regional Office of the World Health Organization in Washington, D. C. Dr. Gonzalez has represented his country at most of the World Health assemblies and the meetings of the Directing Council of the PASB, serving as council chairman at its sixth meeting last autumn in Havana, where he was also a delegate to the First Inter-American Congress on Public Health.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1953 Clinical Meeting, St. Louis, Dec 1-4.

1954 Annual Meeting, San Francisco, June 21-25.

1954 Clinical Meeting, Miami, Florida, Nov. 30-Dec. 3.

1955 Annual Meeting, Atlantic City, N. J., June 6-10.

1955 Clinical Meeting, Boston, Nov. 29-Dec. 2.

AMERICAN ACADEMY FOR CEREBRAL PALSY, Western Hills Hotel, Fort Worth, Texas, Oct 30-31. Dr. Harry E. Barnett, 116 S. Michigan Blvd., Chicago 3. Secretary.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOGY, Palmer House, Chicago, Dec. 5-10. Dr. John E. Rauschkolb, P. O. Box 6565, Cleveland 1, Secretary.

AMERICAN ACADEMY OF OBSTETRICS AND GYNECOLOGY, Netherland Plaza Hotel, Cincinnati, Dec. 14-16. Dr. C. Paul Hodgkinson, 116 South Michigan Blvd., Chicago 3, Secretary.

AMERICAN ACADEMY OF TROPICAL MEDICINE, Brown Hotel, Louisville, Ky., Nov. 12-14. Dr. E. Harold Hinman, University of Puerto Rico, School of Medicine, San Juan 22, P. R., Secretary.

AMERICAN CANCER SOCIETY, New York, Nov. 2-6. Dr. Charles S. Cameron, 47 Beaver St., New York 4, Medical Director.

AMERICAN CLINICAL AND CLIMATOLOGICAL ASSOCIATION, The Homestead, Hot Springs, Va., Nov. 2-4. Dr. Marshall N. Fulton, 124 Waterman St., Providence 6, R. I., Secretary.

AMERICAN COLLEGE OF CARDIOLOGY, Hotel Statler, Cleveland, Ohio, Nov. 6-7. Dr. Philip Reichert, 480 Park Ave., New York 22, Secretary.

AMERICAN PUBLIC HEALTH ASSOCIATION, Hotel New Yorker and Hotel Statler, New York, Nov. 9-13. Dr. Reginald M. Atwater, 1790 Broadway, New York 19, Executive Secretary.

AMERICAN SCHOOL HEALTH ASSOCIATION, Hotel New Yorker, New York, Nov. 9-13. Dr. A. O. DeWeese, 515 East Main St., Kent, Ohio, Secretary.

AMERICAN SOCIETY FOR THE STUDY OF ARTERIOSCLEROSIS, Hotel Knickerbocker, Chicago, Nov. 1-2. Dr. O. J. Pollak, P. O. Box 228, Dover, Del., Secretary.

AMERICAN SOCIETY OF TROPICAL MEDICINE AND HYGIENE, Brown Hotel, Louisville, Ky., Nov. 12-14. Dr. John E. Larsh Jr., University of North Carolina, School of Public Health, Chapel Hill, N. C., Secretary.

ASSOCIATION OF AMERICAN MEDICAL COLLEGES, Hotel Claridge, Atlantic City, N. J., Oct. 26-28. Dr. Dean F. Smiley, 185 N. Wabash Ave., Chicago 1, Secretary.

ASSOCIATION OF MILITARY SURGEONS OF THE UNITED STATES, Hotel Statler, Washington, D. C., Nov. 8-11. Dr. R. R. Sayers, Armed Forces Institute of Pathology, Washington 25, D. C., Secretary.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASES, Hotel Roosevelt, New York, Dec. 11-12. Dr. Clarence C. Hare, 710 West 168th St., New York 32, Secretary.

ASSOCIATION OF STATE AND TERRITORIAL HEALTH OFFICERS, Washington Hotel, Washington, D. C., Nov. 4-7. Dr. John D. Porterfield, 306 Ohio Depts. Bldg., Columbus 15, Ohio, Secretary.

CENTRAL ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS, The Shamrock, Houston, Texas, Nov. 5-7. Dr. Harold L. Gainey, Suite 602, 116 South Michigan Ave., Chicago 3, Secretary.

CONFERENCE OF PUBLIC HEALTH VETERINARIANS, Hotel New Yorker, New York, Nov. 9. Dr. James Lieberman, U. S. Public Health Service, Washington 25, D. C., Secretary.

CONGRESS OF NEUROLOGICAL SURGEONS, Roosevelt Hotel, New Orleans, Nov. 12-14. Dr. B. W. Cannon, 1092 Madison Ave., Memphis, Tenn., Secretary.

INTERSTATE POST GRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA, Palmer House, Chicago, Nov. 2-5. Dr. E. R. Schmidt, 1300 University Ave , Madison 5, Wisconsin, Secretary.

INTER-SOCIETY CYTOLOGY COUNCIL, Philadelphia, Nov. 19-20. Dr. Paul F. Fletcher, 634 North Grand Blvd., St. Louis 3, Secretary.

MIDWESTERN SECTION OF AMERICAN FEDERATION FOR CLINICAL RESEARCH, Congress Hotel, Chicago, Oct. 29. Dr. Robert J. Glaser, 600 S. Kingshighway Blvd., St. Louis 10, Secretary.

NATIONAL ASSOCIATION FOR MENTAL HEALTH, Hotel Carter, Cleveland, Oct. 31-Nov. 2. Dr. George S. Stevenson, 1790 Broadway, New York 19, Medical Director.

NATIONAL SOCIETY FOR CRIPPLED CHILDREN AND ADULTS, Palmer House, Chicago, Nov 12-14. Mr. Lawrence J. Linck, 11 South LaSalle St., Chicago 3, Secretary.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS, New York, Dec. 18. Dr. Franklin M. Foote, 1790 Broadway, New York 19, Executive Director.

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY, Hotel Somerset, Boston, Oct. 28. Dr. Carmi R. Alden, 270 Commonwealth Ave., Boston, Secretary.

NORTH PACIFIC SURGICAL ASSOCIATION, Victoria, B. C., Nov. 20-21. Dr. John A. Duncan, 509 Olive Way, Seattle, Secretary.

OKLAHOMA CITY CLINICAL SOCIETY, Oklahoma City, Oct. 26-29. Miss Alma F. O'Donnell, 512 Medical Arts Bldg., Oklahoma City 2, Executive Secretary.

OMAHA MID-WEST CLINICAL SOCIETY, Hotel Paxton, Omaha, Oct. 26-30. Miss Irene Rau, 1031 Medical Arts Bldg., Omaha 2, Executive Secretary.

PACIFIC NORTHWEST SOCIETY OF PATHOLOGISTS, Eugene, Oregon, Nov. 6-7. Dr. John L. Whitaker, 315 South K St., Tacoma 3, Wash., Secretary.

RADIOLOGICAL SOCIETY OF NORTH AMERICA, Palmer House, Chicago, Dec. 13-18. Dr. Donald S. Childs, 713 East Genesee St., Syracuse 2, N. Y., Secretary.

REGIONAL MEETINGS, AMERICAN COLLEGE OF PHYSICIANS:

MICHIGAN, H. H. Rackham Auditorium, Ann Arbor, Dec. 5. Dr. H. Marvin Pollard, 1313 East Ann St., Ann Arbor, Governor.

MIDWEST—ILL., IND., IOWA, MINN., WIS.—Hotel Schroeder, Milwaukee, Nov. 21. Dr Francis D. Murphy, 536 West Wisconsin Ave., Milwaukee 3, Chairman.

NEW ENGLAND—CONN., MAINE, MASS., N. H., R. I., VT.—Hartford, Conn., Oct. 28. Dr. John C. Leonard, 80 Seymour St., Hartford 15, Conn., Chairman.

NEW JERSEY, Trenton, Nov. 4. Dr. Edward C. Klein Jr., 73 Lincoln Park, Newark 2, Governor.

NORTH CAROLINA, Chapel Hill, Dec. 2. Dr. Elbert L. Persons, Duke Hospital, Durham, Governor.

REGIONAL MEETINGS, AMERICAN RHEUMATISM ASSOCIATION:

OHIO AND WESTERN PENNSYLVANIA, Mayflower Hotel, Akron, Ohio, Nov. 11. Dr. Roger Q. Davis, 1405 Goodyear Blvd., Akron 5, Ohio, Chairman.

SOUTHERN MEDICAL ASSOCIATION, Municipal Auditorium, Atlanta, Ga., Oct. 26-29. Mr. C. P. Loranz, 1020 Empire Bldg., Birmingham 3, Ala., Secretary.

SOUTHERN SURGICAL ASSOCIATION, The Homestead, Hot Springs, Va., Dec. 8-10. Dr. John C. Burch, 2112 West End Ave., Nashville 5, Tenn., Secretary.

SOUTHWESTERN MEDICAL ASSOCIATION, Pioneer Hotel, Tucson, Ariz., Oct. 29-31. Dr. C. C. Stapp, 800 Montana St., El Paso, Texas, Secretary.

WESTERN SURGICAL ASSOCIATION, The Drake, Chicago, Dec. 3-5. Dr. Michael Mason, 154 East Erie St., Chicago 11, Secretary.

FOREIGN

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND, Leeds, England, May 13-15, 1954. Dr. Henry W. S. Wright, 45 Lincoln's Inn Fields, London W.C.2, England, Honorary Secretary.

BRITISH MEDICAL ASSOCIATION, Glasgow, Scotland, July 1-9, 1954. Dr. A. MacRae, B.M.A. House, Tavistock Square, London, W.C.1, England, Secretary.

CANADIAN MEDICAL ASSOCIATION, Vancouver, B. C., Canada, June 18-22, 1954. Dr. T. C. Routley, 135 St. Clair Ave. W., Toronto 5, Ont., Canada, General Secretary.

CONFERENCE OF INTERNATIONAL UNION AGAINST TUBERCULOSIS, Madrid, Spain, Sept. 26-Oct. 2, 1954. Secretariat, Escuela de Tisiologia, Ciudad Universitaria, Madrid, Spain.

CONGRESS OF INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Chateau Frontenac, Quebec, Canada, October 26-29. Dr. A. William Friend, 515 Nome Ave., Akron 20, Ohio, Chairman, Program Committee.

CONGRESS OF INTERNATIONAL ASSOCIATION FOR THE PREVENTION OF BLINDNESS, New York, N. Y., U. S. A., Sept. 12-17, 1954. Professor Franceschetti, 2 Avenue Mirmot, Geneva, Switzerland, Secretary-General.

CONGRESS OF INTERNATIONAL SOCIETY OF SURGERY, Paris, France, May 21-22, 1954. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

INTERNATIONAL CANCER CONGRESS, Sao Paulo, Brazil, July 23-29, 1954. Prof. A. Prudente, 171 rua Benjamin Constante, Sao Paulo, Brazil, President.

INTERNATIONAL CONFERENCE ON THROMBOSIS AND EMBOLISM, Basle, Switzerland, July 15-19, 1954. Dr. W. Merz, Chief Medical Officer, Gynecological Clinic, University of Basle, Basle, Switzerland, Hon. Secretary.

INTERNATIONAL CONGRESS OF CARDIOLOGY, Washington, D. C., and Bethesda, Md., U. S. A., Sept. 12-15, 1954. Dr. L. W. Gorham, 44 East 23d St., New York 10, N. Y., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF CLINICAL PATHOLOGY, Washington, D. C., U. S. A., Sept. 6-10, 1954. Dr. Robert A. Moore, Washington University School of Medicine, St. Louis 10, Missouri, U. S. A., Chairman, Committee on Arrangements.

INTERNATIONAL CONGRESS ON GROUP PSYCHOTHERAPY, Toronto, Ont., Canada, Aug. 12-14, 1954. Dr. J. L. Moreno, Room 327, 101 Park Ave., New York 17, N. Y., U. S. A., Director of Organizing Committee.

INTERNATIONAL CONGRESS OF HEMATOLOGY, Paris, Sept. 6-11, 1954. Dr. Jean Bernard, 86 rue d'Assas, Paris 6e, France, Secretary.

INTERNATIONAL CONGRESS OF HYDROCLIMATISM AND THALASSOTHERAPY, Dubrovnik, Yugoslavia, May 8-16, 1954. Prof. C. Plavsic, Zeleni Venac 1, Belgrade, Yugoslavia, Secretary General.

INTERNATIONAL CONGRESS OF INDUSTRIAL MEDICINE, Naples, Italy, Sept. 13-19, 1954. Professor Scipione Caccuri, Director, Institute of Industrial Medicine Policlinico, Naples, Italy, Chairman, Organizing Committee.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Stockholm, Sweden, Sept. 15-18, 1954. Professor Anders Kristenson, Karolinska Sjukhuset, Stockholm 60, Sweden, Secretary-General.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Sao Paulo, Brazil, April 26-May 2, 1954. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, University of Toronto, Toronto, Ontario, Canada, Aug. 14-21, 1954. For information write: Executive Officer, International Congress on Mental Health, 111 St. George St., Toronto, Ontario, Canada.

INTERNATIONAL CONGRESS OF NUTRITION, Amsterdam, Netherlands, Sept. 14-18, 1954. For information write: Dr. M. van Eekelen, Centraal Instituut voor Voedingsonderzoek T.N.O., 61 Catharynesingel, Utrecht, Netherlands.

INTERNATIONAL CONGRESS ON OBSTETRICS AND GYNECOLOGY, Geneva, Switzerland, July 26-31, 1954. Dr H. de Watteville, Maternité Hôpital Cantonal, Geneva, Switzerland, President.

INTERNATIONAL CONGRESS OF OPHTHALMOLOGY, University of Montreal and McGill University, Montreal, Canada, Sept. 10-11, 1954, and Waldorf-Astoria, New York, N. Y., U. S. A., Sept. 12-17, 1954. Dr. William L. Benedict, 100 First Avenue Building, Rochester, Minnesota, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF ORTHOPEDIC SURGERY AND TRAUMATOLOGY, Berne, Switzerland, Aug. 30-Sept. 3, 1954. For information write: Professor M. Dubois, Isle-Hospital, Berne, Switzerland.

INTERNATIONAL CONGRESS OF PSYCHOLOGY, Montreal, Canada, June 7-12, 1954. For information write: Prof. H. S. Langfeld, International Union of Scientific Psychology, Eno Hall, Princeton University, Princeton, N. J., U. S. A.

INTERNATIONAL CONGRESS FOR PSYCHOTHERAPY, Zurich, Switzerland, July 21-24, 1954. Dr. H. K. Fierz, Theaterstrasse 12, Zurich 1, Switzerland, Secretary General.

INTERNATIONAL GERONTOLOGICAL CONGRESS, London and Oxford, England, July 12-22, 1954. Prof. R. E. Tunbridge, General Infirmary, Department of Medicine, The University, Leeds, England, President.

INTERNATIONAL POLIOMYELITIS CONGRESS, Rome, Italy, Sept. 6-10, 1954. Mr. Stanley E. Henwood, 120 Broadway, New York 5, N. Y., U. S. A., Executive Secretary.

INTERNATIONAL SOCIETY OF BLOOD TRANSFUSION, Paris, France, Sept. 12-19, 1954. For information write: Colonel Julliard, Societe Internationale de Transfusion Sanguine, 53 Boulevard Diderot, Paris 12e, France.

INTERNATIONAL SOCIETY FOR CELL BIOLOGY, Leiden, Netherlands, Sept. 2-9, 1954. Professor Peter J. Gaillard, University of Leiden, Leiden, Netherlands, Secretary.

INTERNATIONAL SOCIETY OF GEOGRAPHICAL PATHOLOGY, Washington, D. C., U. S. A., Sept. 6-10, 1954. Professor Fred C. Roulet, Hebelstrasse 24, Basle, Switzerland, Secretary-General.

JOURNEES MEDICALES, Paris, France, April 21-25, 1954. For information write: Secretariat of the Journees, 12, rue Pierre-Geofroix, Colombes (Seine) France.

LATIN AMERICAN CONGRESS OF OBSTETRICS AND GYNECOLOGY, Buenos Aires, Argentina, Oct. 26-31. For information write: Sociedad Argentina de Obstetricia y Ginecologia, Santa Fee 1171, Buenos Aires, Argentina, S. A.

LATIN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY, Caracas, Venezuela, Feb. 21-25, 1954. Dr. Victorino Marquez Reveron, Centro, Medico, Caracas, Venezuela, Secretary-General.

PACIFIC SCIENCE CONGRESS, Quezon City and Manila, Philippines, Nov. 16-28. Dr. Patrocinio Valenzuela, College of Pharmacy, University of the Philippines, Quezon City, Philippines, Secretary-General.

PAN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY, Mexico, D.F., Mexico, Feb. 28-March 4, 1954. Dr. Pedro Hernandez Gonzalo, 8 No. 358, Vedado, Havana, Cuba, General Secretary.

PAN AMERICAN MEDICAL ASSOCIATION, International Medical Cruise Congress, S. S. Nieuw Amsterdam, Jan. 6-22, 1954. Dr. Joseph J. Eller, 745 Fifth Avenue, New York 22, N. Y., U. S. A., Executive Director.

PAN-PACIFIC SURGICAL CONGRESS, Honolulu, Hawaii, Oct. 7-18, 1954. Dr. F. J. Pinkerton, Suite 7, Young Bldg., Honolulu 13, Hawaii, Director General.

PERSIAN GULF MEDICAL SOCIETY, Dhahran, Saudi Arabia, Dec. 7-8. Dr. N. J. Conan Jr., Department of Internal Medicine, Arabian American Oil Company, Dhahran, Saudi Arabia, Secretary.

SECTIONAL MEETING, AMERICAN COLLEGE OF SURGEONS, London, England, May 17-19, 1954. Dr. Michael L. Mason, 40 East Erie St., Chicago 11, Ill., U. S. A., Secretary.

SOUTH AMERICAN CONGRESS OF ANGIOLOGY, Sao Paulo, Brazil, July 1954. For information write: Dr. Rubens Carlos Mayall, Rua Senador Vergueiro 73, Rio de Janeiro, Brazil, S. A.

WORLD CONGRESS OF INTERNATIONAL SOCIETY FOR THE WELFARE OF CRIPPLES, The Hague, Netherlands, Sept. 13-17, 1954. For information write: D. C. Schaap, Centrale Vereniging, Apeldoorschweg 51, Arnhem, Netherlands.

WORLD FEDERATION OF OCCUPATIONAL THERAPISTS, Edinburgh, Scotland, August 17, 1954.

EXAMINATIONS AND LICENSURE

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various Centers, July 16, 1954. Sec., Dr. Curtiss B. Hickox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Chicago, Nov. 30-Dec. 2. The closing date for acceptance of applications was April 1. *Written.* October 19. The closing date for acceptance of applications was May 1. Exec Sec.-Treas, Dr. William A. Werrell, 1 West Main St., Madison 3.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* New Haven, October. Final date for filing application was July 1. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, Kingshighway and Euclid Ave., St. Louis.

AMERICAN BOARD OF NEUROLOGY AND PSYCHIATRY: *Psychiatry and Neurology.* Dec. 14-15. Applications no longer being accepted. Chicago, April 29-30. Final date for filing application is Feb. 1. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Written examination and review of case histories for all candidates will be held in various cities of the United States, Canada, and military centers outside the continental United States on Feb. 5. Case abstracts are to be sent by the candidate to the Secretary as soon as possible after receiving notification of eligibility to the Part I written examination. Application for reexamination in Part II must be made prior to Feb. 1 of any year. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, January 25-26, 1954. Final date for filing applications was July 1. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago, Jan. 20-22. Final date for filing application was August 15. Final date for filing application for Part I is Nov. 30. Sec., Dr. Harold A. Sofield, 122 S. Michigan Ave., Chicago 3.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Indianapolis, Dec. 4-6. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: *Entire Examination.* San Diego, Oct. 29-31. Final date for receipt of case reports was June 1. Corres. Sec., Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF RADIOLOGY: *Oral. Radiology, Roentgenology, Diagnostic Roentgenology and Therapeutic Radiology.* Chicago, Dec. 6-11. Final date for filing application was July 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part I.* Oct. 28, 1953, March 31, 1954 and Oct. 27, 1954. *Part II.* Chicago, Nov. 9-10; St. Louis, Dec. 14-15; Los Angeles, Jan. 11-12, 1954; Galveston, Jan. 15-16; Washington, Feb. 8-9; Cincinnati, March 8-9; New Orleans, April 12-13; Philadelphia, May 10-11; Boston, June 14-15. Sec., Dr. John B. Flick, 225 S. 15th St., Philadelphia 2.

DEATHS

Phaneuf, Louis Eusèbe ✙ Boston; born in St. Hilaire, Quebec, Canada, Feb. 27, 1884; Tufts College Medical School, Boston, 1913; professor of gynecology at his alma mater; specialist certified by the American Board of Obstetrics and Gynecology; chairman, Section on Obstetrics and Gynecology, American Medical Association, 1943-1944; member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, of which he had been president, American Gynecological Society, New England Obstetrical and Gynecological Society, and the American Radium Society; fellow of the American College of Surgeons; corresponding member of the Société d'Obstétrique and de Gynécologie de Paris and honorary member of the Société Belge de Gynécologie et d'Obstétrique; surgeon-in-chief, gynecologic and obstetric department, Carney Hospital; surgeon-in-chief, department of gynecology, Boston Dispensary; consulting gynecologist, Beth Israel Hospital, Boston, Leonard Morse Hospital, Natick, Attleboro (Mass.) Hospital, Marlboro (Mass.) Hospital, and Henrietta D. Goodall Hospital in Sanford, Maine; consulting gynecologist and obstetrician, Fall River General and St. Anne's hospitals in Fall River, Mass.; consultant, Malden (Mass.) Hospital; in June, 1933, received the doctor of science degree from Tufts College; at the celebration of the centenary of l'Université Laval at Quebec City in 1952 he was granted the degree of doctor of medicine, honoris causa; died Sept. 20, aged 69, following partial gastrectomy for peptic ulcer.

Ferlaino, Frank R. ✙ New York City; born Feb. 1, 1899; Johns Hopkins University School of Medicine, Baltimore, 1927; clinical instructor of public health, New York Medical College, Flower and Fifth Avenue Hospitals; specialist certified by the American Board of Internal Medicine; served during World War I; secretary of the council on postgraduate medical education, American College of Chest Physicians; district counselor for the Industrial Medical Association; member of the American Trudeau Society, American Public Health Association, and the American Heart Association; at one time chairman of the medical advisory board of the state athletic commission; member of the board of directors of the American Research and Education Foundation for Chest Disease; secretary and director of the Common Cold Foundation in Chicago; for many years medical director of the New York offices of General Motors; affiliated with Roosevelt Hospital; served as medical consultant to the Stony Wold Sanatorium in the Adirondacks, Lake Kushaqua, N. Y., and as associate medical director of Schenley Laboratories; associate editor of *Industrial Medicine and Surgery*; died in Long Island College Hospital Sept. 2, aged 54, of myocardial infarction.

Wilkinson, Robert Johnson ✙ Huntington, W. Va.; born in Lynch Station, Va., in 1888; Medical College of Virginia, Richmond, 1912; member of the founders group of the American Board of Surgery; past president of the Southern Medical Association, of which he was vice-president, Southeastern Surgical Congress, the Association of Surgeons of the Chesapeake and Ohio Railway, Cabell County Medical Society, and the Alumni Association of the Medical College of Virginia; president of the West Virginia State Medical Association in 1943 and chairman of the state committee on medical education, the procurement and assignment committee, and the fact finding and legislative committee; fellow of the American College of Surgeons; at the time of his death, chairman of the committee arranging the program for the annual meeting of the International College of Surgeons at White Sulphur Springs in 1954; a director of the World Medical Association; served in the first volunteer medical corps, U. S. Army, during World War I; for many years physician in charge of the Chesapeake and Ohio Railway Employes Hospital; affiliated with St. Mary's Hospital; head of Wilkinson Surgical Clinic; died Sept. 14, aged 65, of coronary occlusion.

✙ Indicates Member of the American Medical Association.

Liva, Arcangelo ✙ Los Angeles; born in Italy in 1887; Eclectic Medical College of the City of New York, 1912; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; fellow of the International College of Surgeons and the American College of Surgeons; for 25 years a member, and formerly president of the state board of medical examiners; past president of the Bergen County Medical Society; affiliated with Hackensack (N. J.) Hospital; attending bronchoscopist, Newark Eye and Ear Infirmary in Newark, where he was affiliated with the Presbyterian Hospital; consultant in ophthalmology and otolaryngology, Bergen Pines, Bergen County Hospital in Ridgewood; in 1935 was awarded the honorary degree of doctor of medicine by the University of Rome; died Aug. 12, aged 66, of cerebral hemorrhage.

Barnes, Frank Haslehurst ✙ Stamford, Conn.; born in Mohawk, N. Y., June 17, 1872; New York Homeopathic Medical College and Hospital, New York, 1896; past president of Fairfield County Medical Society and the Stamford Medical Society; member of the American Psychiatric Association; member of the medical advisory board in Stamford during World War I; specialist certified by the American Board of Psychiatry and Neurology; formerly on the faculty of the New York Post-Graduate Medical School; medical superintendent of Dr. Barnes' Sanitarium; consultant in psychiatry at St. Joseph Hospital and Greenwich (Conn.) Hospital; consulting neurologist at Stamford Hospital, where he died Sept. 14, aged 81, of hypertension, coronary occlusion, and carcinoma of the prostate.

Young, Richard Hart ✙ Omaha; born in Columbus, Neb., Jan. 28, 1904; University of Nebraska College of Medicine, Omaha, 1930; professor of neurology and psychiatry at his alma mater; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association, American Psychopathological Association, and the Central Neuropsychiatric Association; affiliated with Methodist, Lutheran, Children's Memorial, Bishop Clarkson Memorial, and the University of Nebraska hospitals; died in University Hospital, Bellevue Medical Center, New York, Aug. 10, aged 49, of complications following surgery for Parkinsonism.

Blaisdell, Irl Hazard ✙ Syracuse, N. Y.; born in Providence, R. I., March 10, 1911; Boston University School of Medicine, 1935; certified by the National Board of Medical Examiners; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the American Laryngological, Rhinological and Otological Society; clinical associate professor of otolaryngology at the State University of New York College of Medicine at Syracuse; affiliated with City Hospital, Hospital of the Good Shepherd, and Syracuse Memorial Hospital; died near Watertown Aug. 1, aged 42, when his automobile was struck by a train.

Baker, Walter Eugene ✙ Des Moines, Iowa; Drake University College of Medicine, Des Moines, 1907; affiliated with Iowa Methodist, Iowa Lutheran, and Mercy hospitals; died Aug. 29, aged 77, of lobar pneumonia and Parkinson's disease.

Bateman, Wilbert Charles, Zanesville, Ohio; Starling Medical College, Columbus, 1897; past president of the Muskingum County Academy of Medicine; for many years a member and for seven years president of the board of education of Zanesville; formerly city health officer; on the staff of the Bethesda Hospital and the Good Samaritan Hospital, where he died Aug. 29, aged 86, of arteriosclerosis.

Bernheim, Ruth Grace, Cincinnati; Laura Memorial Woman's Medical College, Cincinnati, 1902; for many years affiliated with the Jewish Hospital, where she died Sept. 11, aged 73, of carcinoma of the ovary with metastases.

Borgen, Alfred Edwin, St. Paul; University of Minnesota Medical School, Minneapolis, 1946; served during World War II; died near Duluth Aug. 8, aged 32, of accidental drowning.

Brainard, Benjamin F. ✠ Martin City, Mo.; College of Physicians and Surgeons of Chicago, 1886; College of Physicians and Surgeons, medical department of the Kansas City University, Kansas City, Kan., 1904; an Associate Fellow of the American Medical Association; served on the staffs of Menorah and St. Vincent's hospitals in Kansas City; died Aug. 28, aged 89, of chronic myocarditis.

Brooks, Cadmus Marvin ✠ Little Rock, Ark.; College of Physicians and Surgeons, Little Rock, 1910; clinical professor of anesthesia at the University of Arkansas School of Medicine; member of the American Society of Anesthesiologists; affiliated with the Arkansas Baptist State Hospital, where he died Sept. 2, aged 70, of carcinoma of the colon.

Carrico, Carl C. ✠ Houston, Texas; Baylor University College of Medicine, Dallas, 1928; served during World War II; died in the Veterans Administration Hospital Sept. 7, aged 52, of encephalomalacia and thrombosis of multiple cerebral arteries.

Cook, Edgar Baldwin, Rochester, N. Y.; New York Homeopathic Medical College and Hospital, New York, 1903; served during World War I; for many years associated with the Health Bureau as school physician and mental hygiene examiner; on the staff of the Genesee Hospital; died Aug. 20, aged 71, of arteriosclerosis.

Cowan, John Rice ✠ Danville, Ky.; Harvard Medical School, Boston, 1894; fellow of the American College of Surgeons; affiliated with Ephraim McDowell Memorial Hospital; died Aug. 17, aged 81, of coronary occlusion.

Crowe, Robert Latta, Memphis, Tenn. (licensed in Tennessee in 1914); professor of pharmacology at University of Tennessee College of Medicine and in 1936 appointed dean of the school of pharmacy; died July 26, aged 65.

Cuneo, Peter Joseph ✠ Bakersfield, Calif.; Cooper Medical College, San Francisco, 1911; for many years city health officer; died Sept. 1, aged 69, of cerebral hemorrhage.

Davis, Joseph Edward ✠ Albion, Neb.; University Medical College of Kansas City, Mo., 1900; on the staff of the Boone County Community Hospital; died in Norfolk July 19, aged 79, of mesenteric thrombosis.

Deutsch, Isadore Herman ✠ Oswego, Ill.; St. Louis University School of Medicine, 1925; affiliated with St. Charles Hospital, where he died Aug. 27, aged 56, of carcinoma of the lung.

Dyer, John H. ✠ Warrenton, Mo.; Marion-Sims College of Medicine, St. Louis, 1892; for many years county coroner; died in St. John's Hospital, St. Louis, Sept. 5, aged 85, of arteriosclerotic heart disease and terminal pneumonia.

Eckhardt, Joseph Carl Augustus ✠ Austin, Texas; University of Texas School of Medicine, Galveston, 1908; affiliated with Seton, Brackenridge, and Holy Cross hospitals; for many years physician for the Woman's Confederate Home; died Aug. 27, aged 70, of a heart attack.

Eyman, William George ✠ Pittsburgh; University of Pittsburgh School of Medicine, 1903; fellow of the American College of Surgeons; on the staff of the South Side Hospital; died Aug. 30, aged 81.

Gano, Charles Harkness ✠ Pittsburgh; College of Physicians and Surgeons, Baltimore, 1911; member of the Industrial Medical Association; died in the Presbyterian Hospital Aug. 13, aged 68, of cerebrovascular accident.

Gilbert, George Richardson, Omaha; Omaha Medical College, 1896; died Aug. 27, aged 79, of cerebral arteriosclerosis.

Giordano-Cortese, Modesto ✠ San Francisco; Regia Universita di Napoli Facolta di Medicina e Chirurgia, Italy, 1916; served as an officer with the Italian Army during World War I; affiliated with Notre Dame Hospital and St. Mary's Hospital; died in Yountville, Calif., Aug. 18, aged 62, in an automobile accident.

James, Arthur Gregory Boswell ✠ Bridgeport, Conn.; McGill University Faculty of Medicine, Montreal, Canada, 1927; on the staff of the Bridgeport Hospital; died Aug. 24, aged 57, of acute coronary thrombosis.

Klein, John ✠ Chicago; Rush Medical College, Chicago, 1899; on the emeritus staff at St. Francis Hospital in Evanston, Ill., where he died Sept. 14, aged 83, of lymphosarcoma in the right axilla with metastases to the liver.

Lane, John David ✠ Bennington, Vt.; Bennett Medical College, Chicago, 1909; an Associate Fellow of the American Medical Association; member of the New England Roentgen Ray Society; on the staff of the Putnam Memorial Hospital; died July 31, aged 73.

Lindsay, James Adams ✠ Pittsburgh; University of Pittsburgh School of Medicine, 1909; chief of staff, St. John's Hospital; died Aug. 15, aged 69, of coronary occlusion.

Link, Joseph John ✠ Mattoon, Ill.; Northwestern University Medical School, Chicago, 1920; fellow of the American College of Surgeons; served during World War I; for many years district surgeon for the Illinois Central and New York Central railroads; served as president of the staff at Memorial Methodist Hospital; a director of the Central National Bank; died in St. John's Hospital Aug. 29, aged 57, of hemachromatosis.

Mozley, Charles Almus, Albuquerque, N. M.; St. Louis College of Physicians and Surgeons, 1892; served as health officer of Sandoval County; died in Austin, Texas, Aug. 14, aged 81.

Norton, Alva C. ✠ Rockwell City, Iowa; Rush Medical College, Chicago, 1895; died in Lutheran Hospital in Fort Dodge Aug. 18, aged 81, of carcinoma of the prostate.

Ragan, Romulus C. ✠ Kansas City, Mo.; Medico-Chirurgical College of Kansas City, 1903; on the staff of the Trinity Lutheran Hospital; died in St. Luke's Hospital Sept. 8, aged 86, of acute cholangitis with hepatic abscesses.

Reinsberg, Karl ✠ Mohawk, N. Y.; Philipps-Universität Medizinische Fakultät, Marburg, Prussia, Germany, 1923; president of staff of Ilion (N. Y.) Hospital; died July 30, aged 60, of coronary embolism.

Richardson, Anna Root Mann, Rochester, N. Y.; Boston University School of Medicine, 1901; for many years physician at Smith College in Northampton, Mass.; died in Rochester State Hospital Sept. 9, aged 75, of chronic myocarditis.

Schmidt, Florian Edward ✠ Chicago; Northwestern University Medical School, Chicago, 1905; medical director of the Chicago Heart Association; formerly on the faculty of his alma mater; served on the professional staff of Lederle Laboratories, Inc., and later for nine years with Armour Laboratories; died Sept. 10, aged 69, of myocardial infarction and coronary sclerosis.

Scibetta, Samuel Louis ✠ Erie, Pa.; University of Buffalo School of Medicine, 1917; fellow of the American College of Surgeons; at one time member of the school board; on the staff of Hamot Hospital and St. Vincent's Hospital, where he died Aug. 21, aged 60, of chronic leukemia.

Seyfried, Ernest A. N. ✠ Nazareth, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1929; affiliated with St. Luke's Hospital in Bethlehem, Easton (Pa.) Hospital and Allentown (Pa.) Hospital; died Aug. 17, aged 49, of acute coronary occlusion.

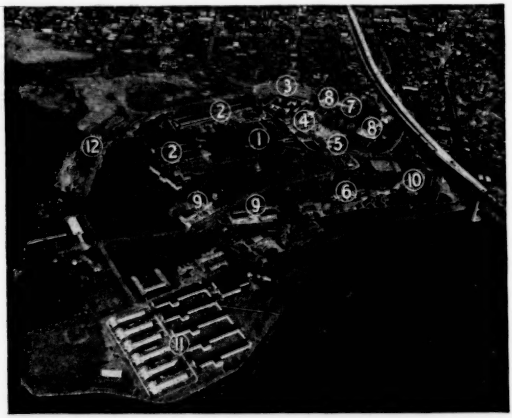
DIED WHILE IN MILITARY SERVICE

Campbell, James McLain ✠ Alexandria, La.; University of Tennessee College of Medicine, Memphis, 1933; for a short time with the Mississippi State Board of Health; served on the staff of the Veterans Administration Hospital; entered the U. S. Army Medical Service as a lieutenant colonel on July 1, 1953; died Aug. 5, aged 43, of coronary thrombosis while at home on a three day pass.

GOVERNMENT SERVICES

NAVY

Naval Hospital at Chelsea.—The Naval Hospital at Chelsea, Mass., where on Oct. 12-14 an important symposium for civilian physicians, as well as military medical officers, was held, was closely associated with early events in the history of our country. The hospital overlooks the Mystic River and historic Charlestown, Mass., and from this point women and children gathered to witness the battle of Bunker Hill in June, 1775. Many of the wounded in that battle were taken across the river, where beneath the trees that shaded what is now the hospital grounds the women dressed the wounds of the victorious Revolutionary soldiers. The area on which the city of Chelsea is built at that time was known as Winnisimmet. The first public ferry in the country was operated in 1631 between Winnisimmet, Charlestown, and Boston, the Winnisimmet landing being on the hospital grounds at the site of the present boat landing. It was not until 1823, however, that the commissioners of naval hospitals purchased 115 acres of land for $18,000 as the site of the proposed Chelsea Naval Hospital, and not until 1832 did Congress appropriate funds for the construction of this hospital. On Jan. 7, 1836, the Chelsea Naval Hospital was completed and placed in commission. The three-story hospital had a capacity of 100 beds. On the anniversary of the 118th year of service of this hospital last June, the historical account of the hospital noted that in 1896 a telephone was installed along with a steam disinfector and that a small room was fitted as a bacteriological, chemical, and microscopic laboratory. The laboratory was reported as "complete including microscope." The first major crisis to confront the hospital came with the pandemic of influenza during World War I when, with the rapid influx of patients, the number of beds was increased to 1,142. The Chelsea Hospital facilities were made available in 1920 to the Veterans Bureau, and in the decade that followed, Veterans Bureau admissions increased until they represented 75% of the total admissions. Again during World War II, the number of patients increased from around 279, before Pearl Harbor, to 2,700 patients, four years later. With minor changes in its routine it was adequate during the recent Korean fighting for all types of admissions from the battle front. The Chelsea Naval Hospital today stands on a windy hill some 112 feet above sea level where it maintains constant vigil over the health of men and women of the United States Navy.



Aerial view of Chelsea Naval Hospital. 1. The main hospital. 2. Additional wards. 3. Women's and children's wards. 4. Auditorium. 5. Red Cross building. 6. Nurses' quarters. 7. Enlisted men's quarters. 8. Waves' quarters. 9. Officers' quarters. 10. Commanding officer's quarters. 11. Maintenance shops. 12. Storerooms.

Atomic Scientist Enters Army.—Dr. Maurice C. Fishler, head of the biological and medical sciences division of the U. S. Naval Radiological Defense Laboratory, San Francisco, has been ordered to military duty as a first lieutenant in the Medical Corps, U. S. Army. He reported for indoctrination at Brooks Army Hospital, Fort Sam Houston, Texas, the middle of October. Dr. Fishler joined the Navy laboratory in 1948 to organize the medical research program and has guided its activities ever since. For several years he has been a member of the Joint Panel on Medical Aspects of Atomic Warfare of the Research and Development Board.

PUBLIC HEALTH SERVICE

Dr. Daft Succeeds Dr. Wilder.—The appointment of Floyd S. Daft, Ph.D., as director of the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, was announced October 12 by the Surgeon General. Dr. Daft, acting director of the institute since the resignation of Dr. Russell M. Wilder last June, has been assistant director and chief of laboratory research since 1951 and a member of the scientific staff of the National Institutes of Health since 1937. He has conducted nutrition studies, particularly on the B vitamins, and his investigations have contributed much to the understanding of dietary deficiencies causing anemia, cirrhosis of the liver, and other metabolic diseases. He was a pioneer in the study of an unidentified substance later shown to be folic acid. Before coming to the National Institutes of Health in 1937, Dr. Daft taught and engaged in research work at Harvard, Yale, the Carlsberg Laboratories, Copenhagen, Denmark, and the University of Rochester.

Personal.—Dr. Joseph O. Dean, formerly associate chief of the Bureau of State Services, Public Health Service, has been named assistant to the medical director of the Bureau of Indian Affairs, Department of Interior. Dr. Dean was appointed to the regular corps of the Public Health Service in 1929.

Regular Corps Examination for Medical Officers.—The Department of Health, Education, and Welfare, U. S. Public Health Service, announces that competitive examinations for the appointment of medical officers to the Regular Commissioned Corps of the service will be held in various cities throughout the country Feb. 2-4, 1954. The examination will include professional written tests, an oral interview, and a physical examination. Completed applications must be in the Washington office by Dec. 24. Appointments will be made in the grades of assistant and senior assistant, equivalent to navy ranks of lieutenant (j.g.) and lieutenant, respectively. Entrance pay is $5,686 for assistant surgeons with dependents, and $6,546 for senior assistant surgeons with dependents. This includes incentive pay, rental, and subsistence allowances. For application forms and additional information, write to: Department of Health, Education, and Welfare, Public Health Service, att.: Chief, Division of Commissioned Officers, Washington 25, D. C.

FOREIGN LETTERS

BRAZIL

Postoperative Jejunal Ulcer.—An etymological study on nomenclature of recurrent ulcers following gastric surgery was made by Dr. Eurico Branco Ribeiro, director of the Sanatorio São Lucas of São Paulo. The term "peptic ulcer," widely used by European authors, is strongly rejected because the ulcer is not caused by peptic digestion. The terms "marginal ulcer" and "anastomotic ulcer" are objected to because the ulcer is not located at the anastomotic ring but generally appears in the jejunum, near the new stoma. The better designation is "postoperative jejunal ulcer."

As a rule the ulcer is believed to be localized in the region most exposed to sudden attrition of the alimentary bolus. The nervous system is assumed to play a part in the pathogenesis, as changes in this system were seen to result in dysfunctions capable of contributing to the development of the ulcer. According to Dr. Ribeiro, in 22 years 28 operations were performed for postoperative jejunal ulcer in a total of 1,367 patients who had previously been treated surgically, i. e., 2.04%. This incidence can be reduced to 1.76% if two patients who both underwent three operations for recurrent ulcer are omitted from the series. Once the alimentary flow has been diverted, resection of the ulcer is not regarded as essential when the excision may impair the blood supply to the small intestine. When possible, however, resection is performed. In some patients vagotomy was done as a supplementary procedure. In one patient who was treated with vagotomy only, the pains recurred within eight months. There were four deaths.

Acute Obstruction in Megacolon.—Megacolon is common in central Brazil. Recently Dr. Oscar Barros Serra Doria pointed out the high incidence (28%) of acute obstruction in patients with megacolon. He believes that volvulus of the sigmoid is rarely the cause of the obstruction. Usually there is accentuated angulation at the rectosigmoid junction. He does not open the abdomen but treats these patients by means of a rectosigmoidoscope and a rectal tube.

Amebic Granuloma in the Large Intestine.—Seven cases of amebic granuloma of the large intestine have been reported by Dr. Haroldo Sodré and Dr. Júlio Croce. They found only nine similar cases in the Brazilian literature although intestinal amebiasis is very prevalent in this country. In the differential diagnosis they consider cancer, tuberculosis, mycosis, syphilis, schistosomiasis, regional enteritis, and paracolic inflammatory tumors. They always use emetine, and in some cases they use penicillin after a course of emetine treatment. This treatment has been very successful, as it cured all the patients in their series. They believe that surgical treatment has proved to be ineffective.

ISRAEL

Seventh International Congress of the History of Science.—The Seventh International Congress of the History of Science opened in Jerusalem on Aug. 4, 1953, and was attended by delegates from all over the world. Prof. F. S. Bodenheimer, of the Hebrew University, as Congress president welcomed the delegates from abroad. He stressed the importance of the study of the history of science for Israel and for the world, and called attention to some of the ancient and medieval scientific relics of the region.

Prof. Ben Zion Dinur, minister of education and culture, delivered the main address at the opening session on "The Value of the History of Science for Public Education." He dealt with the particular qualities of the history of science as a historical science and as an educational subject. "None compares to this science in its potential of education toward the unity of human society, mutual love and international harmony. The history of science includes the history of human thought, the methods of human observations, the ways of formulating conclusions. It is therefore incomparable as a means of developing in the younger generation the ability of independent thinking, of spiritual steadfastness, of constructive criticism, and of moral courage. For there is no courage as worthy of praise and honour as a man's courage to think independently and not in mere imitation of the teachings or traditions of others," he said. Professor Dinur felt convinced that "everything a man acquires from the history of science, in the process of the development and growth of man's spirit of seeking, will be multiplied a hundredfold in the spirit of divine wisdom in man, in the spirit of brotherly love, and of moral courage and civic strength."

Prof. G. Sarton, president of the International Academy of the History of Science, discussed "Science versus the Humanities; the History of Science." He said that the greatest problem of our age is "how to reconcile science with the humanities, how to bridge the growing abyss between well-meaning but ignorant idealists on the one hand, and uneducated technicians on the other." The solution, suggested more than a century ago and still valid, is in the study of the generalities of science and particularly the history of science. Scientific training is absolutely necessary, yet utterly insufficient. A man must be a scientist and a humanist at one and the same time. The New Humanism is an attack on non-humanized scientists whose success would defeat civilization, and on Western scholars who deprecate Eastern efforts. He pointed out the suitability of Jerusalem as a good place to speak of this, for it is really at the very edge of the Arabic and Asiatic worlds.

The medical section was devoted entirely to Jewish or biblical topics. Dr. M. Sherman, president of the Israel Medical Association, discussed the history of medicine in Palestine in the 19th century. There was almost no medical care until 1838, when the European powers, to protect themselves, imposed on the Ottoman Empire a "Sanitary Administration" for purposes of establishing quarantine. The first hospital was founded in Jerusalem in 1843 by the London Society for the Promotion of Christianity among the Jews and the Rothschild Hospital, the first Jewish one, in 1854.

Dr. S. Muntner discussed the life and work of R. Shabbetai Donnolo (10th century), the first European medical writer in Hebrew. Dr. J. O. Leibowitz spoke on the life and work of R. Jacob Zahalon (17th century). Dr. S. H. Blondheim, of the Hadassah Hospital and Hebrew University Medical School, identified the epidemic among the Israelites at Beth Shemesh (I Samuel vi) as the first recorded epidemic of pneumonic plague. It is likely that this disease developed after the Israelites came into contact with the Philistines who suffered from the bubonic type of plague (Black Death) when the latter returned the captured Ark of the Covenant.

Physicians in Israel.—Israel had 3,717 physicians (including 710 women) and 903 dentists (including 359 women) at the end of 1952, the Central Bureau of Statistics and Economic Research revealed in a report based on a census of physicians and dentists. Germany heads the list of countries from which Israel has recruited its medical manpower, 992 physicians and 278 dentists having been trained in German universities and medical schools. More than a third of the physicians (1,278) are concentrated in Tel Aviv; Jerusalem is second in the number of physicians (603) and Haifa third (516). More than a third of the dentists (379) are also concentrated in Tel Aviv; Haifa is second in the number of dentists (127) and Jerusalem third (86). Less than half of the physicians (1,591) are general practitioners, and the remainder are specialists. Internal diseases and children's diseases head the list of the specialties.

The items in these letters are contributed by regular correspondents in the various foreign countries.

New Hadassah Departments in Plastic Surgery and Psychiatry.—The Hadassah Medical Organization will shortly establish departments in plastic surgery, neuropsychiatry, and rehabilitation, Dr. Kalman Mann, director of Hadassah Medical Organization, told the press recently. Prof. M. Rosenbaum of Cincinnatti University has arrived in Jerusalem to consolidate psychiatric work at present being carried out in the Hadassah University Medical School and to plan the new department, which is partially financed by the Schleider Fund, available in instalments of $15,000 annually.

Three physicians sent by Hadassah for training in plastic surgery, due to return soon from the United States, are to form the nucleus of a surgical team. They are Dr. Z. Rosen, specialist in nose and throat operations, Dr. J. Lewin-Epstein, specialist in jaw operations, and Dr. Z. Neumann, specialist in general operations.

The elements of the third new department, covering occupational therapy, physiotherapy, and general rehabilitation, are already in existence and have now been unified under the direction of Dr. E. Adler. Visualizing the hospital as a center of specialized therapy, Hadassah intends to provide daily health care through its local clinics, with the medical student learning from both central and peripheral institutions.

A building to house both a health clinic and cultural activities is to go up at the Beit Mazmil Community Health Center thanks to a donation of $100,000. This prototype health center, catering to 500 immigrant families in a Jerusalem suburb, benefits from the wider specialized care provided by the new hospital departments. Next year, medical students will begin to benefit from the community health center as a pilot plant for all-embracing family care. Instead of dealing with a few isolated cases, each student will be able to observe a number of family cases and thus relate medical problems to their environment. Dr. Mann said that after consulting with the Minister of Health, Mr. Y. Serlin, he had managed to coordinate the Hadassah teaching program with that of the government and other health agencies in Jerusalem.

ITALY

Convention of Rheumatology.—The seventh national convention of the Italian Society of Rheumatology was held in Florence last June under the chairmanship of Professor Villa. The first topic, prevention of rheumatic disease, was discussed by Professor Dogliotti, the director of the University of Turin Institute of Medical Pathology. Clinical observations and epidemiological studies of the last years have made clearer some aspects of the pathogenesis of rheumatic fever. The disease is preceded by respiratory infection due to some strains of hemolytic Streptococcus A in persons who are, in general, constitutionally predisposed to the disease and who live in an environment that favors its development. However, the pathogenetic mechanism that links the streptococcic infection to the complex tissue alterations characteristic of the rheumatic process (swelling and fibrinoid degeneration of the collagen, increased capillary permeability, and Aschoff's granuloma) and that are responsible in their evolution for the severe cardiac complications is not clear.

Although the Streptococcus infection recurs rather frequently in rheumatic patients, often producing clinical flare-ups of the disease, once the rheumatic process has begun it assumes a relatively autonomous course. This is continuous and progressive and is marked by flare-up periods that are improperly called relapses. These relapses are caused not only by the streptococcic infection but also often by other circumstances, such as physical overwork, changes of climate, diet intemperance, and emotional disturbances, that alter the reactive balance of the organism.

Long clinical experience has proved that sulfonamides and penicillin administered in repeated courses prevent the streptococcic infection and therefore the rheumatic disease. This type of prophylaxis can be applied to the many persons who are predisposed to the disease in particular circumstances only, as in epidemics of streptococcic infections. It is mainly indicated for prevention of the so-called relapses. When possible, penicillin should be preferred to the sulfonamides in that it is more active in causing the streptococci to disappear from the mucous membranes of the respiratory tracts without the development of penicillin-resistant strains of the bacteria. In addition, it is less likely to cause such dangerous toxic reactions as granulocytopenia.

Because of the current opinions about the pathogenesis of rheumatic disease, the use of tonsillectomy as a prophylactic measure is criticized. The intervention seems to be indicated only in the forms of chronic suppurative tonsillitis due to hemolytic Streptococcus in which penicillin does not provide a complete and definitive cure of the process. When the rheumatic disease is already in progress, tonsillectomy does not prevent its progress but only minimizes the probability of the so-called relapses.

Considering the great importance of the person's organic constitution for the development of the disease and the many etiological factors that may play a part in the relapses, antiinfectious prophylaxis is not sufficient. The patient's resistance may be increased by improving his diet and his environmental conditions. Besides this, the altered reactivity that is the basis for the pathogenesis of the disease may be corrected with the so-called antirheumatic therapy, namely, with salicylates, aminopyrine (Pyramidon), corticotropin, and cortisone. This therapy has an immediate beneficial effect on the acute manifestations, and, by preventing the exudative phase, it may limit the permanent secondary damages, especially those to the heart. Its preventive action has not been sufficiently proved, however, and studies are now in progress.

Organized and therefore better prophylaxis could be carried out by specialized centers that, in addition to establishing the best prophylactic method, should also be able to make a diagnosis in doubtful cases. A principal duty of the centers should be to spread information about the disease among physicians and the public. They should emphasize the diagnostic criteria and fundamental principles of therapy and prophylaxis, thus making known all the available means of prevention of severe damage to the heart. One of the main obstacles to the fight against rheumatic disease is the meager knowledge of the disease itself and the unsound conviction that it is impossible to prevent it or to influence its evolution and prognosis.

The second topic dealt with specific and nonspecific aspects of immunity in rheumatology. The immunologic study of acute and chronic rheumatic diseases is limited, mainly because of the lack of knowledge about the cause of the disease. Most research workers have admitted the existence of a varying reactivity that is almost unanimously identified as a state of sensitization; this concept, based on clinical data, has been supported despite the lack of exact etiological data.

A study was made to evaluate the conclusions reached in the clinical field and to establish the specific and nonspecific serum reactions of patients with rheumatic disease. Two criteria of research were followed: (1) determination of the specific factors (antigens and antibodies) and nonspecific factors (complement, conglutinin, and opsonin) of the known reactions of immunization, and (2) interpretation of the relation of the action of the antirheumatic drugs to immunization.

Considering the great importance of the nonspecific factors in the antigen-antibody reaction, the speaker studied the complex colloidal alterations of the plasma in rheumatic diseases in relation to the immunologic phenomena. The high antistreptococcic agglutinations that he observed in rheumatic disease was ascribed to an increase of the agglutinating factor of normal serum rather than to the existence of a corresponding antibody titer. The property that rheumatic serum has for nonspecific agglutination confirms the hypothesis that it is really a potentiation of the agglutinins that normally exist before the onset of the disease and not of recently formed immune antibodies.

Immunization reactions became negative following physical modifications of the serum that did not alter the true antibodies. The presence of protein C and similar substances that are not of an antibody nature confirmed the soundness of this concept, which finds the most typical paradigm in the Waaler-Rose reaction. All the tests that the speaker performed proved that the complement titer is increased during the active phase of rheumatic disease.

Considering the activity of antirheumatic drugs from the immunologic standpoint, these studies proved the inhibiting action of sodium salicylate and phenylbutazone (Butazolidin) on agglutination and hemolysis. Moreover, the doses of sodium salicylate that are used in therapy diminish the activity of the complement. Cortisone and corticotropin inhibit the specific and nonspecific factors of immunization. This activity follows a corresponding action on the synthesis of proteins.

The speaker examined also, with particular reference to the aspects of immunization, the favorable effects of jaundice and pregnancy on the rheumatic processes. As for jaundice, he cited the diminution of the complement activity as the expression of a deficiency in the synthesis of plasma proteins. Speaking of the good effects of pregnancy on the disease, he said that during pregnancy experimental anaphylactic shock does not appear, probably because of a decrease of the complement titer. Although it is certain that jaundice and pregnancy influence immunization by differing means, the relation of these processes to the pathogenesis of rheumatic diseases remains to be established.

LONDON

Nonresident Hospital Nurses.—The Standing Nursing Advisory Committee has responded to a request from the Minister of Health for advice and information on the question of whether there were any factors inherent in the work of a hospital nurse that made it necessary or desirable that she live in the hospital in which she worked or in nearby accommodation provided by the hospital authority. The committee considered that, subject to certain reservations in regard to particular grades, there were no factors inherent in a hospital nurse's work that made "living in" necessary. The most important reservations concerned the matron, the ward sister in charge of a ward for acute conditions, and the student nurse, especially in her first year of training. The committee also pointed out that the accommodation provided by a hospital authority for its resident nurses need not necessarily take the form of the traditional nurses' home; a useful alternative would be the acquisition of suitable large houses that could be rented to the nurses as single rooms or apartments.

"The King's Fund."—One of the most interesting, as well as one of the largest, medical charities is the King Edward's Hospital Fund for London, which was founded in 1897 by King Edward VII (then Prince of Wales) for the "support, benefit or extension of the hospitals of London." Its policy has always been to temper charity with caution, and it has never given grants to hospitals or associated institutions unless there was some guarantee that the money would be wisely spent. Such provisos, however, have never been of a negative or obstructive character, because the fund has always been willing to advise the hospital concerned on how to overcome the defects, whether administrative, accounting, nursing, or staff, and so be eligible for the grant that would be forthcoming when evidence was produced that the money would be wisely spent. This sage policy, originally initiated at the express wish of King Edward himself, has had two beneficial effects. One is that over the years the fund has accumulated a wealth of experience in hospital administration, hospital accounting, and nursing organization that has proved to be of value to the hospitals, not only in London but also throughout the country. The other is that the capital resources of the fund now amount to between 6 and 7 million pounds sterling. Expenditures during 1952 totalled £413,760. To outline all the activities of the fund would be impossible, and therefore only a few of its more important, or interesting, activities can be mentioned. These are of intrinsic interest, and in addition show the way in which the voluntary spirit is leavening the hard core of impersonal bureaucracy that now threatens to make the health services of the country very impersonal.

Hospital gardens are a new addition to the list of hospital activities subsidized by the fund, and during last year £3,000 was allotted to hospitals in the East End of London for this purpose. The initiative in this direction came from the hospitals themselves, and all that the fund has done has been to follow its traditional policy of encouraging and facilitating original and deserving ideas produced by hospitals. In order to ensure that the allotted sum is wisely spent, the fund has enlisted the help of both the Royal Horticultural Society and the curator of the Chelsea Physic Graden. An outstanding example of the initiative that the fund wished to encourage was the hospital in Shoreditch in the East End. This hospital has no grounds at all, but a yard has ingeniously been turned into a flower bed by raising a stone wall two feet high round the centre of the yard and filling the enclosed space with earth. Elsewhere in the hospital, flat roofs have been supplied with large boxes of earth. Thus, in the words of the fund's annual report, "though the hospital has no genuine soil, gardens have been provided for the patients, where they can sit and enjoy the sunshine."

Homes for the aged sick have been a special interest of the fund for several years. A sum of £350,000 has been set aside for the provision of 12 homes for the aged sick; these homes are to be under the wing of the hospital service of the National Health Service and are to be used for the accommodation of elderly patients until they become well enough to leave the care of the hospital service. The aim is to overcome the difficulty of so many hospital beds being occupied for long periods by elderly patients who are well enough to get up but not well enough to go home or to a residential home for old persons. Seven of the homes are now open, and all are successful. They are all attached to hospitals interested in old persons. This is considered essential: "The home must be linked with a hospital where the medical staff is actively interested in the care of the elderly. It is only in these hospitals that patients are found who need, as part of their treatment when they are on the road to recovery a stay in such a home." All of the homes are managed by voluntary organizations, mainly by the British Red Cross Society, while the local regional hospital board is responsible for maintenance costs. The medical care in the home is provided by the physician responsible for the elderly in the associated hospital.

Hospital accounting is a subject in which the fund has long and varied experience. It therefore accepted with alacrity an invitation from the Minister of Health to "carry out a complete unit costing of a small number of representative hospitals." This investigation has now been completed, and the principal recommendations are that (*a*) a departmental system of accounting be adopted, based on the units of organization of a hospital, e. g., departments, wards, and services; (*b*) budgets be prepared on the departmental system; and (*c*) all of the accounts be itemized in an income and expenditure account and a balance sheet prepared in accordance with recognized accounting principles. It is claimed that the adoption of this departmental system is the answer to the criticisms that, under the present system, it is not possible to ascertain the cost of maintaining any one of the numerous departments of a modern hospital and that the unit "cost per occupied bed" is futile for purposes of comparison between hospitals. "Under the departmental system a separate account is set up and maintained for each department of the hospital organization and within each such account the expenditure is grouped under significant headings appropriate to the work of the department. Finally, the departmental expenditure is reduced to a cost per unit of service, such units being determined solely by the nature of the service rendered in each case. As, under the new system proposed, the budget is also departmentalized, the budgeted unit cost of each department becomes the 'yardstick' against which its actual cost will be measured." Hospital accounting, it is pointed out, is not mere bookkeeping; it is "an integral part of hospital administration. . . . It is the return obtained for expenditure and not the expenditure itself that is of vital importance, and the real problem of hospital finance, and its control, is to maintain productivity of expenditure at a maximum. A highly centralized rigid financial control of one side only of the equation—payments—is quite inadequate and inappropriate as, under it, success comes to be measured more by the degree to which expenditure is kept within the defined limits, than by the return obtained for the expenditure."

This section of the report concludes with some comments that are probably applicable elsewhere, as well as in the United Kingdom: "During the past half century hospitals have vied with one another in establishing new departments, in opening new clinics and in the over-elaboration of equipment, bringing about duplication and overlapping. In doing so, capital has often been wasted and maintenance costs have increased to unprecedented levels. Has not the time arrived for a backward swing of the pendulum; the time to resolve the balance of functions; the time for hospitals to ask not 'how much more can we get to spend' but 'how much can we reduce our demands?' "

Treatment of Poliomyelitis in Hospital.—A recent memorandum from the Ministry of Health makes recommendations for the arrangements to be made for the treatment of poliomyelitis in hospitals. Wherever practicable, poliomyelitis should be treated in hospital units with a highly trained and experienced team equipped to deal with the disease. Some concentration of cases in such units is essential, if the teams are to have sufficient work to give them the experience they require. The team should include a surgeon or physician competent to deal with respiratory complications and, most important, a senior resident of at least registrar grade, specially trained for this work, who would be available to be called in at a moment's notice to deal with the sudden changes that are a characteristic of the disease. Orthopedic advice should also be available at the unit, together with facilities for physiotherapy in paralytic cases. Nurses should have had training in the management of patients in artificial respirators as well as the commoner techniques. The concentration of cases in suitable units would, of course, be somewhat limited by the undesirability of long ambulance journeys during the acute phase of the disease. Facilities for isolation are more readily provided in hospitals for infectious diseases than in general hospitals, whereas the facilities for treatment are most readily available in general hospitals. Since hospitals for infectious diseases are usually included in groups with general hospitals and are now increasingly used in part as general hospitals, it should be practicable to provide the necessary treatment facilities in any large hospital for infectious diseases chosen to house a poliomyelitis unit. Failing this, a special unit might be provided in a general hospital, if adequate arrangements for isolation are practicable.

When a properly equipped and staffed special unit is not available within a reasonable distance, it may be necessary to arrange special separate isolation accommodation in other hospitals, e. g., general or orthopedic. The hospital selected should be within an hour's ambulance journey, preferably well within this limit.

Except in an emergency, acute cases of poliomyelitis should not be nursed in cubicles attached to children's wards, and all multiple bed isolation wards should have the customary 12 ft. (3.66 m.) between bed centers and a separate staff (if possible, living apart from the other nurses). Acute cases of poliomyelitis among the hospital staff should be segregated. No persons with confirmed cases of poliomyelitis should leave hospital within three weeks of admission. Poliomyelitis patients should not, however, be allowed to return to a susceptible community of children, such as a school, children's home, or day nursery, until six weeks after the onset of the disease.

PARIS

Congress of the International Association for Public Welfare.—The International Association for Public Welfare met on Sept. 21-26, 1953. The agenda included the following topics: recent developments in the field of public welfare, family allowances, evaluation of disablement, and relations between the institutions for public welfare and the medical profession. Permanent technical commissions met from Sept. 14 to Sept. 21. The medicosocial commission dealt with the following points: medical secrecy in public welfare legislation, and polypharmacy. The Commission for Mutual Insurance studied the possible means of contributing to the setting up of systems of social protection in backward countries by means of mutual insurance.

SPAIN

Antituberculous Crusade.—When the problem of tuberculosis in Spain is regarded from the economical and humanitarian points of view, it is evident that the losses the country suffers from this disease are enormous. While the monetary value of human lives cannot be determined, estimations can be made on the basis of the amount of money given to the family of those who are insured by the Compulsory Insurance for Travelers when the insured die in an accident. The amount given to the family for the death of an insured person, regardless of profession, sex and age, is 40,000 pesetas (11 pesetas equals about $1.00). On this basis the annual rate of 30,000 deaths from tuberculosis, represents a loss of 1,200 million pesetas. Adding to this amount the expenses during illness and the loss productive work, a figure of 1,500 millions of pesetas a year lost as a result of tuberculosis is reached. The budget of the National Antituberculous Department has constantly increased from 15 million in 1940 to almost 332 million in 1953.

The amount of money appropriated in the last year is fantastic. When the National Antituberculous Department was established in 1936, a bed in a sanatorium could be made available for 5,000 pesetas per bed and the daily expenses of hospitalization were 5 pesetas. At present, however, the approximate expenses for establishing a bed are 50,000 pesetas and the daily expenses of hospitalization are 28.56 pesetas. At present 280 more dispensaries are needed on the basis of one dispensary for every 100,000 persons. Administration of new antituberculous drugs has not reduced the number of sanatorium beds required. Patients receiving the new antituberculous drugs improve very much but they are not entirely cured and must remain in the sanatoriums.

It is difficult for certain groups and the heads of industrial centers to understand that the main purpose of the National Antituberculous Department is to organize as many sanatoriums and dispensaries as possible, to have in reserve the necessary technical personnel, and to administer the general educational crusade, all of which require the collaboration and economical resources of industrial corporations. For such collaboration and aid, these centers are given a certain number of beds in proportion to the aid they give. Efforts will be made to obtain close collaboration between administrators of health insurance and the National Antituberculous Department. While with the methods used at present these groups and the patients do not receive any actual benefit, they will do so as soon as the groups understand better the needs and privileges of each other.

Several sanatoriums are to be opened in the very near future in the following places: San Sebastian, Ferrol, Castellón de la Plana, El Escorial, Guadarrama, Bejar, and Linares. The sanatorium of Linares is for patients with silicosis. Sanatoriums are under construction in the following places: Logroño, Valladalid, Zaragoza, Burgos, Cadiz, Ciudad Real, Córdoba, Granada, Guadalajara, Huelva, León, Lugo, Alicante, Almería, Badajoz, Navacerrada, Madrid-Tablada, Soria, Teruel, Toledo, Las Palmas, and Tenerife. The efforts carried out in Spain in the antituberculous crusade are commendable. The cost of over 1,000 million pesetas has been provided during a time when the country was not very prosperous. The first and most enthusiastic crusader of this campaign is Dr. José A. Palanca, who is a professor of hygiene of the faculty of medicine of Madrid, the president of the National Antituberculous Department, head of public Health and chief of the Department of Sanitation of the Army, the Navy and the Air Force.

Medical Writing.—The Association of Spanish Physicians has organized a contest for writers and artists with the Premio Blanco award for this year. The award of 5,000 pesetas will be given to the author of the best work on art, history, or literature in relation to medicine. All physicians are invited to participate. Articles should be sent with duplicate typewritten copies, double spaced, before Jan. 1, 1954. They may be written in Spanish, Portuguese, French, Italian, English, German, or Latin. They should be sent with the name and address of the author in a sealed envelope to the Secretaria del Premio Blanco Soler, Fuencarral 113, Madrid, Spain.

CORRESPONDENCE

CHLOROPHYLL DERIVATIVES

To the Editor:—Since my original report on the use of specially prepared chlorophyll derivatives called "chlorophyllins" for the control of breath and body odors in 1950, much controversial literature has appeared. Your editorial is the first comment published by THE JOURNAL that has given my work any fair consideration. There are, however, several mistakes in this material that are the result of quoting persons whose information is outdated or who are misinformed.

According to Von Dobeneck, Willstatter called the mixture of saponification products of chlorophyll, which still contained complex magnesium, chlorophyllins before he identified the components. This term has since been discarded in favor of a more precise description of the saponification products. The removal of magnesium from "chlorophyllin" does not lead to pheophorbides but to chlorins, i. e., chlorin e_6 and rhodin g_7. Most commercial products contain copper complexes of chlorine. The manufacture of these commercial products is in the true sense a very complex procedure, and the analysis of the mixture of chlorins deriving from chlorophyll a and b has been an extremely difficult task, on which Von Dobeneck plans to report soon. P. Rothemund also states that only the magnesium salts of chlorophyll can be called chlorophyllins. I agree that one must insist on the use of correct nomenclature; however, I also believe that this can be accomplished only by discarding obsolete terms and using the universally accepted nomenclature of Hans Fischer. One of your correspondents recently put forth a blanket indictment on all deodorization tests but did not make a specific reference to any particular published test. He is apparently also unfamiliar with Harrisson's paper (read before the Society of Cosmetic Chemists, December, 1952, and published in the *Journal of Cosmetic Chemists*, March, 1953), which completely answers his criticism that professional odor experts cannot transfer their techniques to the examination of breath odors. Dr. Harrisson's paper outlines in detail the care taken to train testers to recognize certain concentrations of different odors on the "stinker" breath.

Brocklehurst in his experiments used preparations of unknown character, and unless he used materials and techniques that are accepted as standard in other papers he cannot be regarded as refuting anyone's work in this field. In in vitro tests there must be intimate contact between chlorophyllins and odors to be neutralized, not just their emanations, as in his bell experiments. Corwin himself is mistaken in his report, because in none of my papers have I tried to explain how chlorophyllins work, and I admit to not knowing. In vitro I know that chlorophyll has no oxygen liberating power and certainly none when ingested. Its systemic action cannot be laid to a bacteriostatic property, because not enough is ingested for this purpose.

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To the Editor:—We believe an editorial in THE JOURNAL, Aug. 29, entitled "Chlorophyll as a Deodorant" contained inaccuracies that should be corrected.

1. A source (K. V. Thimann: personal communication) was given to the effect that "commercial water-soluble chlorophyll preparations . . . are believed to be copper or nickel pheophytins. . . ." This is incorrect, since the water-soluble chlorophyll derivatives used in commercial preparations do not contain the pheophytin fraction.

2. Reference was made to a statement attributed to E. R. Weaver of the National Bureau of Standards to the effect "we have no reason whatever to believe that chlorophyll ever has anything to do with deodorization." This reference, taken out of context, failed to make clear that Weaver's statement applied only to chlorophyll-containing products used as air fresheners. The Bureau of Standards, March 27, 1953, authorized the following statement: "The statement 'we have no reason whatever to believe that chlorophyll has anything to do with deodorization,' appearing in circular 491 of the National Bureau of Standards was intended to relate only to the deodorization of air. The context of the statement clearly indicates the intended meaning. While it was known to the Bureau that chlorophyll and chlorophyll preparations have been applied directly to diseased and injured tissues, the Bureau has no data on such applications and did not intend to express or imply an opinion, either favorable or unfavorable, as to their merits."

3. References were made to a report by Brocklehurst in the *British Medical Journal* and to his conclusions on the deodorant properties of "chlorophyll." A review of the Brocklehurst paper shows that he did not characterize the material used in his work; therefore, since it cannot be duplicated, there is no basis on which to evaluate his findings. Also, either Brocklehurst's description of the odorous substance (methylmercaptan) is in error or he did not produce the material in the fashion he reported, because methylmercaptan is not produced from the starting material he used. If the odorous substance was not methylmercaptan, there is no assurance that the chemical indicator he used would have indicated a change in the odorous substance.

Finally, Brocklehurst employed primarily a nitrogen atmosphere for his experiments. There have been some deodorizing effects reported in the water-soluble chlorophyll derivatives in a nitrogen atmosphere, but these have not been of the same proportion as the effects reported in air. The use of a nitrogen atmosphere minimized the investigator's chances of recording a positive result under normal conditions. Also, in refutation of Brocklehurst's report there has been work done by various American investigators at the University of Alabama, Purdue University, and elsewhere that seem to have been more thoroughly done and whose findings were contrary to those of Brocklehurst.

Perhaps your original editorial was directed at the deodorant properties, as claimed, by various tablets, mouth washes, tooth pastes and similar "chlorophyll"-containing products. However, we believe it should not imply a question of the deodorizing and other properties, within the claims allowed by the Council on Pharmacy and Chemistry, of the ethically promoted Chloresium ointment and solution, which products carry the Council's Seal of Acceptance. These claims have been allowed and these products are accepted for advertising in THE JOURNAL.

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To the Editor:—In a letter "Chlorophyll as a Deodorant," published in your June 27 issue, Prof. K. V. Thimann comes to the conclusion that chlorophyll derivatives have no significant deodorant capacity. I have been working on this problem for more than a year. I presented a paper on the subject at the Federation Meetings in April in Chicago, and I think the data have been ignored by Professor Thimann.

We have investigated the deodorant capacity of well over 70 chlorophyll derivatives. In all instances we used an objective testing method. The procedure reported at the Federation of Societies for Experimental Biology, April, 1953, describes a recirculation system that proved suitable for large samples. Since that time, however, we have found it desirable to check chlorophyll derivative samples of approximately 30 mg. For this purpose we constructed a large water bath in which we could rotate 250 cc. glass tonometers at a constant temperature. In most of our work we used hydrogen sulfide as the

odoriferous gas. The results so obtained were then checked in several instances using mercaptans with identical results.

The procedure is as follows. Thirty milligrams of the chlorophyll derivatives are dissolved in 1 cc. of distilled water. This solution is then drawn by vacuum into the clean dry tonometer. The tonometer is then evacuated to a standard pressure and attached to a bag containing approximately a 5% hydrogen sulfide mixture in air. The valve of the tonometer is opened, permitting a predetermined volume of the gas mixture to flow into the evacuated tonometer. The tonometer is then placed in the water bath at 34 C and slowly rotated for 30 minutes. At the end of that time the gas in the tonometer is pulled through an iodine solution and then back-titrated with thiosulfate. Since the concentration of hydrogen sulfide in the tube before contact with the chlorophyll derivative was known, it can be compared with the value obtained after contact. The difference between the two values, that is, the percentage reduction in hydrogen sulfide, is taken as a measure of deodorant capacity.

The procedure described above was designed to give approximately 50% reduction with a standard chlorophyll derivative because we wanted to test the effectiveness of different samples. Allow me to point out that the more potent derivatives give as much as a 70% reduction in the concentration of the hydrogen sulfide upon immediate contact with the chlorophyll solution. I think these experiments indicate conclusively that the chlorophyll derivatives are capable of deodorizing, since they effectively alter odoriferous gases such as hydrogen sulfide and the mercaptans.

We also carried out a few in vivo experiments in which we determined the concentration of scatol in the feces of dogs given chlorophyll derivatives orally. In every instance there was a significant decrease in scatol concentration, which supports the dramatic clinical findings in colostomy patients.

There is no question but that the subjective procedures that are in current use for evaluating deodorants leave much to be desired, and there is also no question but that chlorophyll products have been promoted in very dubious ways. However, when the chlorophyll derivatives are made available at the right place, in the right form, and in adequate concentration they do function, I believe, as extremely effective deodorants.

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BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Foods and Drugs Differentiated By Intended Use.—The defendant was charged with a violation of the medical practice act in that she had administered drugs while holding a license to practice one of the limited branches of medicine. From a judgment of conviction, the defendant appealed to the Supreme Court of Ohio.

After examining and treating a patient by chiropractic methods, the defendant advised the patient about her diet and said that she should drink fennel and sage tea during the day, that she should drink only boiled water or Minnehaha Water, that certain vegetables were infested with spray poison, and that she should drink either raw milk or goat's milk. The defendant then gave the patient two little packets of pills, an order blank with a designation GE 8, and a list of vegetables that could be eaten without washing. The two packets of pills contained only lactose, or milk sugar, with a small amount of common salt, and the preparation GE 8, purchased by the patient from the Basic Endocrine Sales Company, contained "cholesterol, cerebrocides and lacithin, brain substance material along with some vegetable fiber."

The defendant contended, among other things, that the trial court erred in charging the jury that "fennel and sage are used in the United States Pharmacopoeia as drugs and, therefore, come within the definition of drugs," and that it would take judicial notice that fennel and sage were not foods. The defendant also claimed as error the action of the trial judge when he answered in the affirmative the jury's interrogatory as to whether fennel and sage used as tea are still considered drugs.

The Supreme Court pointed out that there was no evidence with reference to anything in either the official "United States Pharmacopoeia" or the official "National Formulary." Furthermore, it was admitted that the 1950 edition of the "United States Pharmacopoeia" failed to disclose the listing of fennel, although it was listed in the "National Formulary," and that sage was not listed in either the pharmacopoeia or the formulary. Nevertheless it was contended by the state that the judge could take judicial notice of the contents of these publications and that he could inform himself in any way that may seem best to him concerning subjects of which he may take such notice.

Assuming, said the Supreme Court, that the trial court may take judicial notice of what is listed in the pharmacopoeia and formulary, it is still not sufficient under the definition of "drug" contained in the General Code, that the article merely be recognized in the pharmacopoeia or formulary. To make such an article a "drug" it must, in addition, be intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or animals. To constitute any article a "drug" that is not so listed, it too must be intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or animals. Therefore, continued the Supreme Court, the charge that an article is a drug, simply because it is listed in the pharmacopoeia or formulary, without qualifying it by its intended use, is an incorrect statement under the law of Ohio, and the court committed prejudicial error in so charging. There is no question that certain articles may be either food or drugs, depending on their intended use.

The state contended that the defendant practiced medicine when she advised the patient to drink only boiled water or Minnehaha Water and alleged that distilled water is listed in the latest edition of the "United States Pharmacopoeia." Assuredly, said the court, boiled or spring water would not of itself be a drug under the statutory definition unless it was intended for the uses outlined in the statute.

The defendant insisted that all the advice and articles that she gave to the patient either concerned or were articles of food, and that there was no evidence to contradict this. In fact, the trial court indicated to the jury that peas, lima beans, corn, potatoes, carrots, raspberries, blueberries, bananas, rye bread, raw sugar, goat's milk, raw milk, and Minnehaha Water are foods, although fennel and sage are not. As we have said, concluded the Supreme Court, there is not a scintilla of evidence to dispute the statements of the defendant that all the articles with which the present case is concerned are foods, and there is not a scintilla of evidence that they were intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease.

In view of the fact that there was positive testimony that all articles given or recommended to the patient were foods, that they were not intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, and that the articles in question can not be said to be food as a matter of law, the Supreme Court held that there was an entire lack of proof to sustain the verdict. Accordingly the judgment of conviction against the defendant was reversed. *State v. Winterich, 105 N. E. (2d) 857 (Ohio 1952).*

Hospitals in General: Injury to Patient Following Collapse of Adjustable Chair.—The plaintiff filed suit for personal injury suffered by her while a patient in the defendant hospital and alleged the injury was caused by the defendant's negligent failure to furnish a safe appliance and equipment for her use. From a judgment for the plaintiff, the defendant appealed to the supreme court, appellate division, that reversed the judgment. The plaintiff, therefore, appealed to the Court of Appeals of New York.

The plaintiff entered the defendant hospital as a patient after an accident in which she had suffered a fracture of the neck

of the right femur where it enters laterally into the right hip socket of the pelvic bone. When surgery had accomplished the pinning of the fractured bone in apposition and in good alignment and a period of convalescence had passed, the plaintiff was permitted at times to sit in a wheel chair to which two separately operated leg rests were attached that, when not in use, hung down on either side of the chair front. When either leg rest was in use, it could be raised to a horizontal position at the level of the chair seat and thus afford support for a disabled leg when extended. When so elevated, the leg rest could be held stationary in the desired position by a ratchet, or notched locking device, on the under side. The function of the locking device was described by the defendant's medical director as "a safety measure on it so that, if undue pressure is placed upon that leg rest, with the vertical leg rest out like that, it will go down. The reason for that is, if you don't have a safety valve release, and you put undue pressure on it way out like that, you would throw the whole thing clear way forward."

Immediately before the accident in the defendant hospital, the plaintiff was seated in a wheel chair of the type described. Her left leg was flexed so that her left foot rested on a lower cross piece that served as a foot support. Her disabled right leg was extended and rested on the right leg rest, then elevated to a position almost horizontal with the chair seat. According to her testimony, which stands uncontradicted, the plaintiff, in an effort to alter the position of her body as a means of gaining a more comfortable posture, raised herself slightly by pressing down on the arms of the chair and by exerting slight pressure on her left foot. As she did so, the right leg rest "went down" tipping the chair forward slightly and causing her right foot to strike the floor in such a manner as to break the bone again at the right hip socket and to dislodge from its imbedded position the surgical nail that had been inserted to hold the fractured femur in place.

We are required, said the Court of Appeals, to consider the evidence in the aspect most favorable to the plaintiff and to accord to her the benefit of every favorable inference that can reasonably be drawn from it. We cannot, therefore, agree with the appellate division that ". . . the plaintiff failed to prove facts from which the jury could find any actionable negligence on the part of the defendant hospital." In addition to evidence to which reference has been made, there was testimony by the plaintiff's husband that while he was in his wife's hospital room on the night before her injury, he noticed a wheel chair near her bed and, while examining it casually, he observed that, when he "took hold" of the right leg rest and "set it in on a notch and pressed on it," it would "snap down" with very little pressure and that the left leg rest held better. Although the plaintiff was lying in her bed when her husband was "fussing" with the wheel chair, as she termed it, and although the chair was the one involved in the accident that befell her the next day, there is no evidence that before the accident she was informed or had reason to know that the right leg rest when elevated would drop down under light pressure. In fact, there is no evidence that at the time the right leg rest dropped down the plaintiff had exerted upon it even slight pressure.

As a patient, said the Court of Appeals, the plaintiff could rightfully expect from the defendant hospital the exercise of reasonable care in the selection and maintenance of equipment furnished for her use. Such standard of reasonable care required of the defendant that the wheel chair provided for plaintiff would be in a safe condition—as to structure and maintenance—for the use to which it was to be put. On the record before us, said the Court of Appeals, the decisive question was whether there was any substantial evidence that the proximate cause of plaintiff's injuries was a failure by the defendant properly to perform the administrative act mentioned above. We think, the court concluded, that there was such evidence which presented a question of fact for determination by a jury.

Accordingly the judgment in favor of the defendant hospital was reversed and the cause was remanded for a new trial. *Holtfoth v. Rochester General Hospital, 105 N. E. (2d) 610 (New York 1952).*

Indemnity Insurance: Extent of Coverage of Malpractice Insurance Policy.—This was an action for a declaratory judgment to determine the obligation of the plaintiff insurance company to one of its policy holders. The trial court held that no obligation under the policy existed, but this finding was reversed by the court of appeals. The company then appealed to the Supreme Court of Ohio.

A Mrs. Hirssig commenced an action against Michota, a chiropodist, to recover damages for personal injuries attributed to his negligence. She alleged that she was a patient of Michota and went to his office to receive treatment for a foot ailment; that she entered one of the treatment rooms and, following his instructions, attempted to seat herself in a metal hydraulic chair designed for the occupancy of patients; and that, after she placed her left foot on the chair and attempted to raise herself into it as she had done on previous occasions, the chair suddenly rotated to the left, causing her to lose her balance and fall to the floor, whereby she was injured. It was charged that Michota was negligent in failing to "lock" the chair before directing Mrs. Hirssig to get into it, in failing to give warning that the chair was unlocked and would rotate if stepped upon, and in failing to maintain the chair in a safe condition for use by patients.

Michota held a policy of liability insurance in the American Policyholders Insurance Company, which provided that the company would defend each claim and suit "arising out of the practice of the insured's profession as specified herein, and to pay the expenses incurred in the defense of such claim or suit in addition to the applicable limit of liability of the policy." It also provided that the insurance company would pay on behalf of the insured all sums that the insured becomes obligated to pay because of injuries resulting from professional services rendered or that should have been rendered. The insurance company contended that, under the policy, its liability either "to defend" or "to pay" was strictly limited to those injuries that might arise out of the actual rendition of professional services by the insured and that the allegations of the petition in the case of Hirssig v. Michota did not disclose an incident within the protection of the policy. Michota, on the other hand, contended that the language of the policy is in broad and comprehensive terms, and that, in conformity with the well-established and universally recognized rule, any doubt or ambiguity with respect to the meaning of the phraseology employed in the policy must be resolved in favor of the insured and against the insurer, which prepared and issued the policy and collected a premium therefor, and, further, that the injury described by Mrs. Hirssig in her petition did bring the case within the policy provisions.

This court, said the Supreme Court, is of the opinion that the insurance company is liable under its policy. The policy is entitled "Professional Liability Policy" and nowhere in the language relied on is the liability of the insurer restricted to "malpractice" or, by the wording of the policy, is liability thereunder confined to a failure on the part of the insured to exercise that standard of professional skill in the treatment of patients prescribed by law. When Mrs. Hirssig entered Michota's office and in a treatment room thereof began to follow his precise instructions in preparing herself for his professional ministrations, the relationship of patient and physician was clearly established. Her claimed injuries, according to the allegations of her petition, were due to the negligence of the chiropodist in failing to maintain apparatus employed by him in the practice of chiropody in a safe condition for her use as a patient. The injury described was one "arising out of the practice of the insured's profession." Maintaining the treatment chair in a proper and safe condition for the accommodation of patients was a service or duty directly connected with the practice by Michota of his profession as a chiropodist. The insurer, concluded the Supreme Court, is therefore obligated to defend the action of Mrs. Hirssig against Michota and, in the event of a verdict and final judgment against him, the insurer is liable to pay, on the doctor's behalf, such sum as may be within the limits of the policy. The judgment of the court of appeals against the plaintiff insurance company was therefore affirmed. *American Policyholders Insurance Company v. Michota, 103 N.E. (2d) 817 (Ohio, 1952).*

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

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Neurotoxicity of Streptomycin Group of Drugs.—Winston presents clinical and investigative data on cochlear and vestibular complications resulting from streptomycin and dihydrostreptomycin therapy. Damage to the cochlear and vestibular mechanisms caused by the streptomycin group of drugs is always bilateral, and the deafness is of the perceptive type. Streptomycin frequently damages the vestibular apparatus and rarely damages the cochlear apparatus, while dihydrostreptomycin frequently causes deafness as well as severe damage to the vestibular apparatus. The incidence of these complications is directly proportional to the size of the daily dose of the drug and to the number of days it is administered. With streptomycin, deafness is usually preceded by tinnitus as a warning symptom. It practically never occurs with daily doses of less than 3 gm. Deafness and vestibular damage are more abrupt with dihydrostreptomycin, and these complications may become severer or be entirely delayed for some time after therapy has been discontinued. If the complications are slight or moderate, the hearing impairment and vestibular dysfunction may ultimately improve. Audiometry and vestibular turning tests should be carried out from time to time during therapy and again within six months after therapy has been discontinued. While streptomycin appears to have a much more frequent neurotoxic effect upon immature rats than adult rats and while it has been shown to cross the placenta, no neurotoxic effect upon the fetus has thus far been noted. Pregnancy, apparently, does not contraindicate the use of streptomycin. In Ménière's disease streptomycin does not eliminate the recurrent attacks of vertigo, but renders them much less severe. Because it attacks the central vestibular mechanism and possibly other brain structures as well, streptomycin should not be used for this purpose.

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Ophthalmologic Diagnosis of Meningiomas of Sphenoidal Ridge. T. P. Kearns and H. P. Wagener.—p. 221.

Limitations in Use of Gamma Globulin in Poliomyelitis.—Hammon points out serious limitations to the use of gamma globulin in prophylaxis of poliomyelitis. These are due in part to the fact that gamma globulin is an immunizing agent giving only temporary, passive protection. More important are the difficulties presented by the disease itself. Only 1 of 100 or more infections with poliomyelitis virus is clinically recognized. Undiagnosed, primary infection leads to multiple secondary infections among which may be one with clinical manifestations permitting diagnosis. This epidemiological concept leads to what may actually be the most effective use of gamma globulin: It should be used in the family at the time of exposure of the family members. When this occurs through inapparent infection, it cannot be recognized, but the primary infection in the family must frequently be manifested as an undiagnosed case. The severer a poliomyelitis epidemic becomes, the higher will be the proportion of undiagnosed, febrile illnesses that are actually poliomyelitis. Injection of family members at this time should be prior to the onset of approximately 75% of all secondary cases, as in measles. Expecting modification of the involvement in the earliest cases and prevention of most of the later ones, use of gamma globulin in such families should give excellent results. Epidemiological and immunologic evidence strongly supports the hypothesis that this is a more selective method of administra-

tion than indiscriminate and essentially simultaneous mass immunization of all children in all epidemic communities. The more selective approach to families, based on diagnosis or suspect diagnosis by a physician, could be handled largely by physicians in private practice with referral of others to a health department clinic. Indiscriminate, mass community injection would include not only the same children wastefully injected under the suspect case contact method because the wrong index diagnosis had been made but also all other children in all families in which not even a suspect illness occurred and would include many families in which known and suspect cases had occurred weeks before and had probably left the family solidly immune. Lack of direct, experimental evidence should not restrict administrative practice from doing what epidemiological and immunologic evidence strongly suggests is reasonable.

Sarcoidosis in Armed Forces.—The occurrence of sarcoidosis is reported in 17 members of the United States Army in Europe. White exceeded Negro patients in a ratio of 9 to 8. Presenting symptoms were chest pain in four patients and hilar adenopathy, with or without pulmonary infiltration in five. Chills, fever, anorexia, nausea and vomiting, sore throat, edema of legs were observed occasionally. Exclusive of the usual lymphadenopathy, there was a small number of physical findings, such as swollen painful joints, edema of legs, and enlargement of liver and spleen. No patient had uveoparotid, skin and bone involvement. Sarcoidosis is recognized as a generalized reaction to some unknown stimulus. The complicating factor of many known stimuli showing the same pathological response makes its diagnosis complex. Involvement cannot be determined clinically on history and physical examination, since there may be no symptoms referable to the organ and no enlargement or tenderness, although biopsy may show pronounced involvement. Liver needle biopsy, which propably provides representative evidence of sarcoidosis and is relatively harmless, was made in 15 patients and yielded positive results in 11, which again emphasized the frequent early involvement of this organ. Liver function tests showed rather poor coordination with positive biopsy results. Persistently abnormal laboratory evidence should be followed by repeated biopsies, especially if there is a consistently positive and rising sulfobromophthalein (Bromsulphalein) retention. The variability of the course of sarcoidosis and poor response to most therapeutic agents cloud its prognosis and treatment.

American Journal of Obstetrics & Gynecology, St. Louis

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*Cervical Carcinoma in Situ: Difficulties in Differential Diagnosis. J. Hoffman, D. M. Farell and G. A. Hahn.—p. 354.
Estrogen Metabolism in Human Pregnancy: Study with Aid of Deuterium. W. H. Pearlman, M. R. J. Pearlman and A. E. Rakoff.—p. 370.
Male Hormone in Treatment of Menopause. R. I. Walter.—p. 375.
Simplified Method for Sterilization of Female. T. N. Evans.—p. 393.

Pregnancy and Subacute Bacterial Endocarditis.—Questionnaires were sent to 300 hospitals, each with 2,000 or more deliveries per year. Replies received from 102 revealed a total of 113 cases of subacute bacterial endocarditis preceding or complicating pregnancy. In addition, seven case reports were collected from the British literature. The report is based on 120 cases, 85 with healed subacute bacterial endocarditis and 35 complicated by and cured of this disease during pregnancy. The maternal mortality for the series was 6.6%. Pregnancy following healed subacute bacterial endocarditis is contraindicated for the first six months following the clinical cure. During this period, lack of stabilization of the cardiac reserve results in an increased incidence of congestive failure and an increased maternal mortality rate. If pregnancy occurs during this phase, therapeutic abortion without tubal ligation is indicated during the first trimester. The advisability of childbearing is determined by a critical evaluation of the underlying cardiac lesion in cases in which subacute bacterial endocarditis has been cured for periods longer than six months. The incidence of recurrence during pregnancy is similar to that noted in the healed, nonpregnant person. The treatment of subacute bacterial endocarditis is as successful in the pregnant as in the nonpregnant patient. Early diagnosis is the key to successful treatment. The prenatal care and conduct of labor are similar to those in any patient with heart disease. Cesarean section should be performed only for obstetric indications. Routine intrapartum and postpartum use of antibiotics is advocated to prevent the recurrence of the disease.

Differential Diagnosis of Carcinoma in Situ.—There is agreement that cervical carcinoma passes through an intraepithelial phase before it begins to invade the stroma. The morphological characteristics of carcinoma in situ include marked anaplasia, hyperchromatism, polynucleosis, disparity in the size, shape, and staining quality of the nuclei, disturbance in the nuclear-protoplasmic ratio, increased mitotic activity, abnormal mitotic figures, loss of polarity, loss of layering and disorderly arrangement, and an intact basement membrane. With apparently so clear-cut a picture, it might be expected that this entity would offer little difficulty. In practice, however, there is considerable confusion as to the proper application of the term "carcinoma in situ" and consequent uncertainty as to the management of lesions so designated. This is largely attributable to the facts that the epithelium rarely fulfills all the cytological criteria and the lesions have been seen to regress or at least not to progress to invasive state, though untreated. The authors summarize observations on 4,152 cervical biopsy specimens obtained between 1930 and 1946. This number included nine invasive carcinomas with previous biopsy specimens, among which one true intraepithelial carcinoma was found. The findings among 4,187 cervical biopsy specimens obtained between 1946 and 1952 are presented, with particular emphasis on six cases diagnosed "carcinoma in situ" and followed by repeat cervical biopsies without treatment other than the repeat biopsies, which, to date, showed the lesions to be reversible. The desirability of a policy of watchful waiting in the doubtful case, particularly if the patient is young, and the comparative safety of such a policy are stressed. The "in situ" problem is likely to continue to plague the gynecologist. Findings among more than 8,000 cervical biopsy specimens support the conservative point of view, which maintains that true intraepithelial carcinoma is an exceptional finding with the limited diagnostic facilities at our disposal today. It is hoped that future research will make it possible to recognize beginning cervical carcinoma with certainty and to distinguish it from the benign carcinomimetic lesions that cause considerable confusion.

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American Journal of Surgery, New York

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Id.: II. Presence of Bartonella Bacilliformis in Peripheral Blood of Patients with the Benign Form. A. Herrer.—p. 645.

Id.: III. Experimental Infection of Squirrels. A. Herrer.—p. 650.

*Histoplasmin and Coccidioidin Testing in Philippine Tuberculosis Hospital. C. Halde and A. C. Reyes.—p. 655.

Testing with Histoplasmin and Coccidioidin in a Philippine Tuberculosis Hospital.—Studies were made on 824 patients in a tuberculosis hospital in the Manila area. Most histoplasmin surveys have been made along with tuberculin surveys. Since most of the Filipino patients on whom this study was conducted had demonstrable acid-fast bacilli in their sputums, tuberculin testing was not done. None of the 824 patients showed a reaction to coccidioidin, but 26 patients (3.15%) had a reaction to histoplasmin. Each reacting patient was retested two or three times and gave a consistent reaction. In the endemic areas for coccidioidomycosis in California, progressive coccidioidal granuloma with a high mortality rate has been found to develop in some Filipinos. Therefore, the absence of reactors to coccidioidin in this survey indicates that coccidioidomycosis is probably not present in the Philippines.

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*Comparative Study of Streptomycin and Dihydrostreptomycin in Pulmonary Tuberculosis. S. S. Cohen, L. Johnsen, M. R. Lichtenstein and W. J. Lynch.—p. 229.

*Comparative Study of Streptomycin and Dihydrostreptomycin in Pulmonary Tuberculosis. S. C. F. Mahady, F. L. Armstrong, F. Beck and others.—p. 238.

Streptomycin and Dihydrostreptomycin in Pulmonary Tuberculosis.—A cooperative study for a controlled clinical appraisal of streptomycin and dihydrostreptomycin in the treatment of tuberculosis was carried out in eight hospitals. Of 294 patients with pulmonary tuberculosis who were treated in hospitals in Minnesota, North Carolina, Illinois and California, according to the plan, 145 were given streptomycin and 149 dihydrostreptomycin. One gram of streptomycin or dihydrostreptomycin in a single daily intramuscular injection plus 12 gm. of *p*-aminosalicylic acid was given orally in divided doses. The standard duration of treatment was 120 consecutive days plus or minus one week. Follow-up observations were continued for a minimum of six months. Results showed that both streptomycin and dihydrostreptomycin are valuable agents in the chemotherapy of amenable forms of tuberculosis in properly selected patients. It was not possible to determine any significant difference in the therapeutic efficacy of the two drugs. When administered in combination with *p*-aminosalicylic acid, neither type of streptomycin was associated with the emergence of a significant incidence of drug-resistant infection. Vestibular toxicity, which generally occurred relatively early in the course of treatment, was more frequently observed with streptomycin. Auditory toxicity, which tended to occur relatively later, was more frequently due to dihydrostreptomycin. Although usually ranging from subclinical to moderate in degree, the auditory disturbance can be of serious proportions. It can be progressive or it may appear belatedly after chemotherapy has ceased. High tone (audiometric) loss or complaint of sustained high-pitched tinnitus is the first indication of side-effects and should always be considered significant. Allergic responses to streptomycin were not infrequent and were occasionally severe. Allergic reactions were rarely observed when dihydrostreptomycin was employed.

Comparative Study of Streptomycin and Dihydrostreptomycin. —Of 141 patients with pulmonary tuberculosis admitted to four New York State tuberculosis hospitals which participated in the cooperative study reported in the same issue of this journal, 73 received dihydrostreptomycin and 68 streptomycin. The dosage of streptomycin or dihydrostreptomycin was 20 mg. per kilogram of body weight per day, rather than the 1 gm. dose per day used in the other four hospitals. The patients also were given 12 gm. of *p*-aminosalicylic acid orally daily. A small number of patients received only the basic 120 consecutive days of chemotherapy (±7 days), and the vast majority received drug therapy for longer periods. No difference in the therapeutic efficacy of streptomycin and dihydrostreptomycin was discernible when they were administered for 120 days and when the results were evaluated at that time. No significant difference was observed in the frequency of emergence of drug-resistant strains, which with either drug was less than 8%. The small percentage of patients in each original group who were still sputum positive after one year of treatment emphasizes the impropriety of drawing conclusions about the drug resistance studies with respect to the two drugs. Ototoxicity of the two drugs is of considerable im-

portance. Vestibular disturbances occurred with either drug, but were more frequent, of greater severity, and often of earlier occurrence with streptomycin. Auditory disturbances were relatively uncommon with streptomycin and, when present, were usually less severe. Auditory disturbances are more to be expected when dihydrostreptomycin is used. They were usually mild or slight in severity when the drug was given for only 120 days. They were of greater severity and frequency when administration was prolonged beyond six months of daily treatment. The auditory disturbances occasionally progressed even after therapy was stopped, or they appeared some time after the conclusion of chemotherapy. The earliest changes of ototoxicity detected with either drug were usually tinnitus and/or high-tone loss of relatively mild degree.

Arkansas Medical Society Journal, Fort Smith

50:29-42 (July) 1953

"Comments on the Practice of Medicine." R. B. Robins.—p. 29.
Surgical Treatment of Mitral Stenosis and Report of Three Cases. J. A. Buchman and W. M. Hamilton.—p. 32.

Cancer Research, Chicago

13:477-544 (July) 1953

Conditioned and Autonomous Neoplasms: Review. J. Furth.—p. 477.
Highways and Byways of Cancer Research. S. P. Reimann.—p. 493.
Nucleic Acids and Tumor Genesis in Broad Bean. R. M. Klein, E. M. Rasch and H. Swift.—p. 499.
Effect of Dose and Hormones on Tumor Production in Rats Given Emulsified 9,10-Dimethyl-1,2-benzanthracene Intravenously. R. P. Geyer, J. E. Bryant, V. R. Bleisch and others.—p. 503.
Effect of Ethionine on Tumor Growth and Liver Amino Acids in Rats. H. M. Levy, G. Montañez, E. A. Murphy and M. S. Dunn.—p. 507.
Effect of 2,4-Dinitrophenol and of Fluoride on Oxidations in Normal and Tumor Tissues. P. Siekevitz and V. R. Potter.—p. 513.
In Vitro Demonstration of an Antigen in Red Blood Cells of C3H Mice. L. Adelsberger and H. M. Zimmerman.—p. 521.
Mammary Tumor Agent in Extracts of Frozen and Unfrozen Mammary Cancers. J. J. Bittner and D. T. Imagawa.—p. 525.
Metabolism of Benzidine in Rat. R. K. Baker and J. G. Deighton.—p. 529.
Effect of Limited Food Intake on Survival of Mice Bearing Spontaneous Mammary Carcinoma and on Incidence of Lung Metastases. A. Tannenbaum and H. Silverstone.—p. 532.
Substrate Utilization by Ehrlich Mouse Ascites Carcinoma Cells. R. W. McKee, K. Lonberg-Holm and J.-A. Jehl.—p. 537.

Diseases of Chest, Chicago

24:123-244 (Aug.) 1953

Development of Psychological Program in Tuberculosis Hospital. B. M. Stewart, R. R. Casady and D. Salkin.—p. 123.
Reliability of Chest Roentgenography and Its Clinical Implications. J. Yerushalmy. —p. 133.
"Initial Foci," a Special Group of Minimal Tuberculosis, Prognosis and Treatment. E. Hedvall.—p. 148.
Diagnosis in Congenital Heart Disease. D. F. Downing.—p. 157.
•Intralobar Pulmonary Sequestration. G. Boyd.—p. 162.
Complications of Enzymatic Debridement in Pulmonary Tuberculosis with Bronchopleural Fistula. L. W. Jones, S. H. Dressler, J. Denst and J. B. Grow.—p. 173.
•Cavitation Within Bland Pulmonary Infarcts. P. H. Soucheray and B. J. O'Loughlin.—p. 180.
Phthisiogenetic Considerations Based on Tomographic Analysis of 320 Consecutive Cases of Localized Pulmonary Tuberculosis in Adults. H. Adler.—p. 191.
Clinical Problem of Infected Cystic Disease of Lung. R. H. Meade and R. A. Rasmussen.—p. 205.
Prevention of Iodism in Bronchography by Use of ACTH: Case Report. F. R. Park, R. T. Cronk and G. E. Cronk.—p. 219.
Evaluation of Middlebrook-Dubos Hemagglutination Test in Tuberculosis. R. M. Howard, A. G. Brees, M. G. Henderson and R. S. Berk.—p. 226.

Intralobar Pulmonary Sequestration.—Six cases of a congenital lung anomaly of teratological and clinical interest are reported in three boys and three girls. The anomaly consists of a portion of a displaced lung tissue in the chest cavity with hypoplastic alveoli and dilated bronchi that give the lung its honeycombed or cystic appearance. This displaced lung is the recipient of a systemic vascular supply usually from the aorta. It has been referred to as intralobar sequestration since Price's paper on the first case of this type diagnosed at operation in 1948. Of the author's six cases some were diagnosed preoperatively and the others by examination of the specimen after excision and by the finding of an aberrant artery when the portion of the lung was removed. The condition is probably due to the amputation of a primordial lung bud by an aberrant artery occurring in the 4 to 14 mm. embryo. Clinical findings consisted of cough with little or no sputum and recurrent bouts of fever and were occasionally accompanied by hemoptysis. The radiographic changes demonstrating the true nature of the case are a mass often of considerable density, at times homogenous and cystic areas usually visualized in it or in nearby portions of the lung. The mediastinum is in the midline. The bronchogram usually shows a mass into which the opaque contrast medium does not penetrate; occasionally it may enter for a short distance. The demonstration of a complete bronchial tree, diseased or otherwise, extraneous to the mass, is important. Attention to this detail will prevent removal of a mass and leaving behind bronchiectatic portions of the lung with the false assumption that a complete excision was made. The only effective therapy is surgical removal of the abnormal lung and any infected normally developed lung. Three cases are cited in which the whole lung was involved in the process. The question was raised whether such a result could not ensue rather than agenesis when earlier more massive portions of the bronchial tree are amputated in the embryo.

Cavitation Within Bland Pulmonary Infarcts.—Of 100 cases of pulmonary infarction reviewed by the author, the occurrence of pulmonary infarction due to bland emboli showing roentgenologic evidence of pulmonary cavitation is reported in four men and one woman between the ages of 26 and 64. It was established that cavitation within a pulmonary infarct might occur in the absence of pyogenic abscess formation. This phenomenon of aseptic necrosis with cavity formation is unusual and is significant only in that it should be recognized as one of the sequelae of pulmonary infarction. Mere presence of pulmonary cavitation did not seem to be a grave prognostic sign. Antibiotic therapy apparently controls infection sufficiently so that these necrotic infarcts may heal without surgical treatment. The diagnosis of pulmonary infarction could be made much more frequently by relying on the recognized clinical and roentgenological signs of the condition.

GP (J. Am. Acad. Gen. Practice), Kansas City, Mo.

7:1-168 (July) 1953

ACTH and Cortisone in Treating Blood Disorders. I. H. Manning Jr. —p. 34.
Simple Office Treatment of Diabetes. L. Steine.—p. 45.
Anxiety or Hyperthyroidism. J. A. Smith and D. W. Chapman.—p. 49.
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Hawaii Medical Journal, Honolulu

12:423-506 (July-Aug.) 1953. **Partial Index**

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This Era of Anxiety. R. J. McArthur.—p. 443.
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Third Generation Syphilis. C. V. Caver.—p. 448.

Iowa State Medical Society Journal, Des Moines

43:251-318 (July) 1953

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Journal of Applied Physiology, Washington, D. C.

5:725-820 (June) 1953

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Secretion of Electrolytes in Thermal Sweat. T. T. Amatruda Jr. and L. G. Welt.—p. 759.

Reliability of Metabolism Measurements by Closed Circuit Method. F. L. Harmon.—p. 773.

Physical Properties of Human Lungs Measured During Spontaneous Respiration. J. Mead and J. L. Whittenberger.—p. 779.

Lung Volume Restriction, Hypoxia and Hypercapnia as Interrelated Respiratory Stimuli in Normal Man. J. C. Mithoefer, C. D. Stevens, H. W. Ryder and J. McGuire.—p. 797.

Comparison of Relationship of Respiratory Minute Volume to pCO_2 and pH of Arterial and Internal Jugular Blood in Normal Man During Hyperventilation Produced by Low Concentrations of CO_2 at 1 Atmosphere and by O_2 at 3 Atmospheres. C. J. Lambertsen, R. H. Kough, D. Y. Cooper and others.—p. 803.

Excretion and Retention of Two Modified Gelatins in Normal Human Beings. P. K. Siiteri and G. P. Highland.—p. 814.

Journal Clin. Endocrin. & Metab., Springfield, Ill.

13:891-1020 (Aug.) 1953

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Neutral Steroids in Urine of Patient with Luteoma of Ovary. L. L. Engel, R. I. Dorfman and A. R. Abarbanel.—p. 903.

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Metabolism of Testosterone by Neoplastic Human Prostate. H. M. Lemon, H. H. Wotiz and T. Robitscher.—p. 948.

Use of Desoxycorticosterone Trimethylacetate in Treatment of Addison's Disease. G. W. Thorn, D. Jenkins, W. L. Arons and T. F. Frawley. —p. 957.

Cervical Mucus in Amenorrhea. G. Di Paola and M. Lelio.—p. 974.

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Journal of Clinical Nutrition, Allentown, Pa.

1:267-342 (May-June) 1953

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Iron Deficiency in Infancy and Childhood. N. J. Smith and S. Rosello. —p. 275.

Time Factors in Utilization of Mixture of Amino Acids (Protein Hydrolysate) and Dextrose Given Intravenously. R. Elman.—p. 287.

Dietary Modifications of Plasma Cholesterol and Phospholipid Levels in Diabetic Patients: Effects of Mixed Diets High in Vegetable Fat. G. C. Cochrane, G. D. Michaels and L. W. Kinsell.—p. 295.

Intravenous Treatment of Pernicious Anemia with Vitamin B_{12}. L. M. Meyer, R. McInerny and N. D. Ritz.—p. 299.

Use of Oral Fat Preparations in Medicine. A. Grollman.—p. 302.

Journal of Experimental Medicine, New York

98:99-194 (Aug.) 1953. **Partial Index**

Effect of Infection with M. Tuberculosis and of Tuberculin Shock on Succinic Dehydrogenase Activity of Guinea Pig Tissues. S. N. Chaudhuri and S. P. Martin.—p. 99.

Observations Concerning Production and Excretion of Cholesterol in Mammals: X. Factors Affecting Absorption and Fate of Ingested Cholesterol. M. Friedman, S. O. Byers and E. Shibata.—p. 107.

Variation in Functional Power of Human Sweat Glands. V. P. Dole and J. H. Thaysen.—p. 129.

Effect of Ketone Bodies and Other Metabolites on Survival and Multiplication of Staphylococci and Tubercle Bacilli. R. J. Dubos.—p. 145.

Intracellular Forms of Pox Viruses as Shown by Electron Microscope (Vaccinia, Electromelia, Molluscum Contagiosum). W. H. Gaylord Jr. and J. L. Melnick.—p. 157.

Journal of Infectious Diseases, Chicago

93:1-110 (July-Aug.) 1953

Bacteriophage Typing of Staphylococci. J. E. Blair and M. Carr.—p. 1.

Hepatitis in Laboratory Mice. M. D. Lackey, P. L. Eichman and W. P. Havens Jr.—p. 14.

Tubercle Bacillus Lipopolysaccharide as Adjuvant in Production of Experimental Allergic Encephalomyelitis in Rabbits. B. H. Waksman and R. D. Adams.—p. 21.

Antibacterial Effect of Elemental Sulfur. L. Libenson, F. P. Hadley, A. P. McIlroy and others.—p. 28.

Directed Leucocyte Migration in Response to Infection and Other Stimuli. S. S. Elberg and P. Schneider.—p. 36.

Reduction of Inorganic Substances by Yeasts: I. Extracellular Reduction of Sulfite by Species of Candida. W. J. Nickerson.—p. 43.

Relationship of Antigenic Characteristics of Streptococci and Specific Antibody Responses Following Streptococcal Infections. R. W. Quinn, C. V. Seastone and R. W. Weber.—p. 57.

*Role of Laundry in Recontamination of Washed Bedding. B. D. Church and C. G. Loosli.—p. 65.

Relation of Tricarboxylic Acid Cycle to Bacterial Infection. L. J. Berry and R. B. Mitchell.—p. 75.

Action of Mucin in Promoting Infections: Effect of Previous Injection of Mucin and of α Tocopherol in Peanut Oil. H. P. Lambert, H. Smith and J. Richley.—p. 93.

Influence of Strain, Sex and Age of Mice on Infection with Plasmodium Berghei. J. Greenberg, E. M. Nadel and G. R. Coatney.—p. 96.

Studies on Respiratory Metabolism of Balantidium Coli. M. Agosin and T. von Brand.—p. 101.

Immunologic Characterization of Mucinolytic Enzyme of Vibrio Cholerae. K. E. Jensen.—p. 107.

Recontamination of Washed Bedding in Laundries.—Church and Loosli describe bacteriological studies that were carried out in two laundries (one hospital and one commercial). The air, wash and rinse waters, and textiles before washing and after rinsing and ironing were examined to determine the source of organisms found in the laundered materials. It was found that the laundry processes were efficient in removing bacteria from the fabrics during washing but that the materials became recontaminated during water extraction in the spin dryer or while hanging in the laundry to dry. This was shown by the fact that the air, during the sorting of linen and other activities, became highly contaminated with bacteria that settled out on woolen blankets hanging in the laundry and on fabrics at the folding table. In addition, large numbers of air-borne bacteria were drawn through the spin dryers during the process of water extraction and impinged on the washed textiles. Although the ironing process killed large numbers of these organisms, many survived. The surviving organisms were mainly nonhemolytic alpha streptococci and Micrococcus albus and aureus, which are potential human pathogens. It is not inconceivable that so-called "clean linen," which has become recontaminated with air-borne organisms dispersed from unwashed bedding, may be the source of initiating serious infections when placed again on hospital beds. The authors discuss measures to prevent the recontamination of washed bedding.

Journal of International College of Surgeons, Chicago

20:1-132 (July) 1953

*Multivalvular Heart Disease and Simultaneous Surgical Correction. H. E. Bolton, C. P. Bailey, W. L. Jamison and K. V. S. Rao.—p. 1.

Gas Cysts of Intestine: Report of Case. L. H. Appleby.—p. 11.

*Percutaneous Femoral Artery Aortography: Its Use in Evaluation of Retroperitoneal Masses. E. C. Peirce II.—p. 16.

Tuberculosis of Mammary Gland. W. J. Moore and J. F. Hamilton. —p. 29.

Traumatic Cataract Surgery in Children: Needle-Hook Technic. O. R. Wolfe.—p. 38.

Preserved Rib Cartilage: Satisfactory Foreign Body Implant to Reconstruct Microgenic Chin. L. W. Eisenstodt.—p. 47.

Developmental Abnormalities of Head and Neck. W. G. McEvitt.—p. 54.

Surgical Diseases of Biliary Tract. R. C. Giles.—p. 70.

Management of Hemorrhage from Genital Tract During Late Pregnancy, Labor and Puerperium. R. J. Pieri.—p. 77.

Bronchoscopic Resuscitation of the Newborn. J. J. Donlon.—p. 94.

Gastric Malignant Disease. R. H. Abrahamson.—p. 99.

Method for Clinical Study of Common Bile Duct After Choledochostomy. J. A. Sterling and R. Goldsmith.—p. 106.

Multivalvular Heart Disease and Simultaneous Surgical Correction.—Bolton and associates operated on 843 lesions of the mitral valve and on 74 patients with aortic stenosis. The 74 patients with aortic lesions included 28 with associated mitral valvular lesions that were treated concomitantly. The authors

discuss the techniques utilized for mitral insufficiency, such as mitral commissurorrhaphy or valvular suturing. In some cases of mitral valvular disease, stenosis and insufficiency are associated. In such instances the commissurotomy is done first. The regurgitation may diminish owing to this valvular mobilization to such a point that valvular suturing is not necessary. This is determined by palpating the regurgitant jet that strikes the finger in the left atrium during each ventricular systole. In the estimation of these authors 12 to 15 cc. per heartbeat is the upper limit of regurgitation that can be readily tolerated. When necessary, the valvular suturing is carried out after commissurotomy. The early attempts at aortic commissurotomy consisted of inserting a dilator through the wall of the left ventricle and advancing the instrument to the level of the aortic valvular ring. The dilator was then expanded in order to dilate the valvular orifice. The dilating mechanism was one which expanded in an elliptic form. There was a tendency for the dilated portion to slip out of the valvular orifice, which resulted in an inadequate dilation. This instrument was abandoned when the Bailey aortic dilator was developed, which proved to be very satisfactory. When there is coexisting mitral valvular and aortic valvular disease, the problem of which lesion should be treated first is baffling. If there is mitral obstruction present and this is relieved, the persistence of aortic obstruction will probably result in left ventricular engorgement if the aortic obstruction is not relieved in short order. The authors generally do the mitral operation first. If one's experience in the treatment of aortic stenosis is somewhat limited, it might be wise to perform the aortic commissurotomy first. Then, if it becomes necessary to abandon further operation at this time, the mitral procedure can be performed at a later date. The authors state that of the 28 patients subjected to concomitant treatment of multivalvular heart disease 6 died. Of the 22 survivors, 20 were improved.

Percutaneous Femoral Artery Aortography for Evaluation of Retroperitoneal Masses.—Evaluation of retroperitoneal masses is frequently difficult. Arteriography, venography, and retroperitoneal oxygen injection can increase information about such masses. Arteriography is the most important of these, and can be done either by direct translumbar puncture of the aorta or by various catheterization methods of introducing radiopaque dye into the abdominal portion of the aorta. These methods of catheterization utilize surgical cut-down on the femoral artery, which is not only difficult and time consuming but also involves danger of thrombosis of the femoral artery. Peirce used the percutaneous femoral artery approach to catheterize the abdominal portion of the aorta, thus making practical a simple, accurate, and versatile second method of abdominal aortographic investigation. The method allows accurate injection of a contrast medium with the patient in any position. It is fairly readily learned and is economical of personnel and equipment.

Journal of Investigative Dermatology, Baltimore

20:401-490 (June) 1953

Antibiotics and Their Action on Pathogenic Fungi: I. Penicillin and Streptomycin. F. Raubitschek.—p. 401.
Erythromycin Ointment in Treatment of Pyodermas. H. M. Robinson Jr. and I. Zeligman.—p. 405.
Treatment of Granuloma Inguinale with Erythromycin. H. M. Robinson Jr. and M. M. Cohen.—p. 407.
Zirconium-Pyribenzamine Cream for Prophylaxis of Rhus Dermatitis. R. E. Strauss and C. R. Bruck.—p. 411.
Histology and Cytochemistry of Human Skin: IV. Eccrine Sweat Glands. W. Montagna, H. B. Chase and W. C. Lobitz Jr.—p. 415.
Relationship of Spread of India Ink to Hair Cycle in Rabbit Skin. J. S. Strauss and A. M. Kligman.—p. 425.
Experimental Histamine Pruritus: II. Nature; Physical and Environmental Factors Influencing Development and Severity. F. E. Cormia and V. Kuykendall.—p. 429.
Fungistatic and Fungicidal Activity of Vegetable Essential Oils and Their Components. X. Vilanova and M. Casanovas.—p. 447.
Relationship of Streptococcus Fecalis to Psoriasis. M. M. Robinson. —p. 455.
The Vitamin, Amino Acid and Growth Requirements of Genus Microsporum. E. S. Bereston.—p. 461.
Growth in Developing Chicken Embryo of Filtrable Agent from Verruca Vulgaris. J. A. Bivins.—p. 471.

Journal Lab. and Clinical Medicine, St. Louis

42:1-164 (July) 1953

Changing Trends in Medical Intern-Resident Education. R. M. McKean. —p. 1.
Metabolism of Dextran—A Plasma Volume Expander: Studies of Radioactive Carbon-Labelled Dextran in Dogs. R. Terry, C. L. Yuile, A. Golodetz and others.—p. 6.
Chloride "Space" and Total Exchanging Chloride in Man Measured with Long-Life Radiochloride, Cl^{38}. S. A. Threefoot, G. E. Burch and C. T. Ray.—p. 16.
Some Theoretic Considerations of Electrolyte Space Measured by Tracer Method in Intact Man. G. E. Burch, C. T. Ray and S. A. Threefoot. —p. 34.
Study of Sodium, Potassium, and Chloride Contents of Thermal Sweat of Man Collected from Small Isolated Areas of Skin. G. S. Berenson and G. E. Burch.—p. 58.
Study of Urinary pH to Hemoglobin and Its Modification by an Antiadrenergic Drug (Regitine) and by Changes in Serum Sodium Level. J. U. Schlegel, J. J. Betheil and A. L. Bloch.—p. 78.
Effect of Some Serums on Titer of Rh Antibodies. Method for Detection of Rh Sensitization. E. P. Leroy and W. Spurrier.—p. 85.
Relation Between Heparin Blood Levels and Blood Coagulation Times. F. C. Monkhouse, R. L. MacMillan and K. W. G. Brown.—p. 92.
Disturbance of Vitamin B_6 Metabolism in Pregnancy: II. Influence of Various Amounts of Pyridoxine Hydrochloride Upon Abnormal Tryptophane Load Test in Pregnant Women. M. Wachstein and A. Gudaitis. —p. 98.
Analysis of Alveolar-Arterial Oxygen Pressure Gradient in Mitral Stenosis. S. G. Blount Jr., M. C. McCord and others.—p. 108.
Plasma Lipoprotein Changes Induced by Mild Local Cold Injury. R. F. Redmond, L. J. Milch and W. W. Calhoun.—p. 112.
Corticosteroid Excretion in Liver Disease. H. P. Schedl, K. Ditto and W. B. Bean.—p. 116.
Studies of Liver Function Tests: III. Dependence of Percentage Cholesterol Esters Upon Degree of Jaundice. L. Zieve.—p. 134.
Failure of Antistreptolysin to Protect Against Streptococcal Infection. M. Hamburger and H. M. Lemon.—p. 140.

Journal of Neurosurgery, Springfield, Ill.

10:331-442 (July) 1953

Intracarotid Injection of Papaverine in Cases of Cerebrovascular Thrombosis: Preliminary Report. I. S. Cooper and A. Morello.—p. 331.
Cytologic Diagnosis of Tumor Cells in Cerebrospinal Fluid. C. P. Larson, J. T. Robson and C. C. Reberger.—p. 337.
Experimental Cerebral Concussion. E. L. Foltz, F. L. Jenkner and A. A. Ward Jr.—p. 342.
Intra-Arterial Pressures in Neck and Brain: Late Changes After Carotid Closure, Acute Measurements After Vertebral Closure. L. Bakay and W. H. Sweet.—p. 353.
Intraspinal Neoplasms in Cervical Region. J. H. Webb, W. McK. Craig and J. W. Kernohan.—p. 360.
Carotid Angiography with Urokon, Using Chamberlain Bi-Plane Stereoscopic Angiographic Unit: Report of 100 Cases. P. Lin, F. Murtagh, H. Wycis and M. Scott.—p. 367.
Surgical Management of Cerebritis Complicating Penetrating Wounds of Brain. A. M. Meirowsky and G. R. Harsh III.—p. 373.
Use of Frozen Cranial Bone Flaps for Autogenous and Homologous Grafts: In Cranioplasty and Spinal Interbody Fusion. K. H. Abbott. —p. 380.
Disorders of Electrolyte and Water Metabolism Following Brain Surgery. I. S. Cooper.—p. 389.
*Relative Accuracy of Electroencephalography, Air Studies and Angiography: In Series of 200 Mass Lesions. F. A. Martin, J. E. Webster and E. S. Gurdjian.—p. 397.
*Treatment of Aneurysms of Circle of Willis. G. Norlén and H. Olivecrona.—p. 404.

Diagnosis of Intracranial Mass Lesions.—The relative accuracy of electroencephalography, pneumoencephalography, ventriculography, and angiography as aids in diagnosis of verified, selected intracranial mass lesions was studied in 200 consecutive patients. No single method proved adequate in the localization of all types of intracranial mass lesions. Of the 224 preoperative electroencephalograms, which were recorded in 198 patients, 168 were abnormal. The diagnosis was aided by the electroencephalogram in 101 cases, the tracing indicating the site or cranial fossa of involvement; but encephalography can be considered only as a useful adjunct to other diagnostic methods. Projected electroencephalographic abnormalities may be falsely interpreted as focal abnormalities, and focal abnormalities tend to become generalized with progression of the disease. Of the 90 pneumoencephalograms performed by the removal of the cerebrospinal fluid and replacement with room air through the lumbar route, employed in the diagnosis of 82 cases, 46 were recorded as abnormal. Thirty of the tumors were localized by this method, an accuracy of 36%. Pneumoencephalography is valuable in the localization of hemispheric mass lesions and is the procedure of choice with tumors at the

midline base. Of the 100 ventriculograms performed by the replacement of ventricular fluid with room air through two burr openings in the cranium on 96 patients, 4 were diagnostic failures because of insufficient ventricular filling. In 88 the findings were abnormal, and in 86 they were diagnostic. Ventriculography is the most useful method in the localization of any intracranial mass lesion; it has a general accuracy of 90%. It is the only method, with the exception of vertebral angiography, that is helpful in the diagnosis of posterior fossa masses. Fifty-seven carotid angiograms were performed on 57 patients. Of the 57 masses, 31 were localized exactly. Masses of the anterior two-thirds of the hemispheres and about 50% of those at the midline base may be localized by carotid angiography.

Treatment of Aneurysms of the Circle of Willis.—The results of operations for bleeding aneurysms of the circle of Willis depend on the time in relation to bleeding at which surgical intervention is performed. Of 15 patients operated on in the acute stage between a few hours up to 22 days after the onset of subarachnoid hemorrhage caused by saccular aneurysms of the circle of Willis, 8 died. Good recoveries followed in six patients, and in one patient hemiplegia began to develop the day after operation and became permanent. The procedure employed was ligature of the neck of the aneurysm in 12 patients, wrapping the aneurysm with muscle in 1, and trapping of the aneurysm in 2. In five of the eight fatal cases pronounced vasospasm was present. The authors' impressions from these experiences are that, when massive hemorrhage has occurred, no operation is likely to save the patient, that as a rule it is useless to operate unless the patient survives the first two days, and that the circulation of the brain is profoundly disturbed during the first two or three weeks following hemorrhage, this disturbance being the result both of the increase in intracranial pressure and the vasoconstriction almost invariably present in these cases. During the first three weeks after hemorrhage the results of all types of operations are about the same as with conservative treatment. To the credit side of the surgical intervention must be added that, if the neck of the aneurysm has been clipped, the patient is protected against further hemorrhage. If early operation is performed, efforts must be made to overcome the vasospasm. Of 63 patients with saccular aneurysms of the circle of Willis operated on during the quiescent period following the acute stage, 2 died. The procedure employed was ligature of the neck of the aneurysm, usually with a clip, in 48 patients, wrapping the aneurysm with muscle in 8, trapping the aneurysm in 2, and exploration in 5. Operations after the patient has recovered from the initial hemorrhage are to be considered as a prophylactic measure aimed at preventing further hemorrhage. Clipping of the neck of the aneurysm or trapping meets the conditions stipulated for operations performed after the patient's recovery from the initial hemorrhage. Mortality and morbidity after clipping of the neck of the aneurysm, performed three to four weeks after the last attack of bleeding, is very low and protection against future hemorrhage is excellent.

Journal of Thoracic Surgery, St. Louis

26:1-110 (July) 1953

*Lobar Obstructive Emphysema in Infancy Treated by Lobectomy. H. Sloan.—p. 1.
Mucocele, Congenital Bronchiectasis, and Bronchiogenic Cyst. B. H. Ramsay and F. X. Byron.—p. 21.
*Aortic Commissurotomy. H. B. Larzelere and C. P. Bailey.—p. 31.
Cardiopulmonary Function Tests. V. O. Björk.—p. 67.
Leiomyoma of Esophagus: Report of Case with Successful Enucleation of Tumor. J. Zaslow and S. O. Krasnoff.—p. 86.
Giant Intramural Leiomyoma of Esophagus: Case Report. L. J. Kenney. —p. 93.
Intrathoracic Meningocele Not Associated with Neurofibromatosis. A. D. Sears, R. S. Clayton and E. Siebel.—p. 101.
Results of Supervoltage Roentgenotherapy of Esophageal Carcinoma. F. Buschke and S. T. Cantril.—p. 105.

Lobectomy in Lobar Obstructive Emphysema in Infancy.—Severe obstructive emphysema, most marked in a single lobe, was observed in four infants. In two the left upper lobe was involved; in two, the right middle lobe. Lobectomy was performed successfully in each of the infants; the youngest was 6 days old and the oldest 8 months. The removed lobes showed marked, generalized emphysema. Infection was not present, and no bronchial obstruction was found. It is believed that the obstructive emphysema was due to a check valve mechanism produced by abnormal flaccidity of the bronchi. Each of the infants was improved by lobectomy. All, however, had respiratory symptoms following discharge. In two of the infants there was roentgenographic evidence following operation of emphysema in other portions of the lungs. The bronchial abnormality probably involved other portions of the bronchial tree. Sloan reviews reports on this type of emphysema and stresses that the infants observed at his clinic had labored respirations, wheezing cough, and cyanosis. The symptoms were usually believed to be related to a respiratory infection, but none of the infants had such an infection when examined. The use of antibiotics did not produce improvement. On physical examination there was hyperresonance to percussion over the involved hemithorax, with diminution of breath sounds on auscultation. An expiratory wheeze was often present when the infants cried. The emphysematous lobe filled the entire hemithorax. There was compression of adjacent lung tissue. The mediastinum was shifted to the opposite side. The hemidiaphragm on the affected side was depressed. Shift of the mediastinum with respiration could be demonstrated in two of the infants. In none of the infants was there clinical or roentgenographic evidence of regression of the emphysema prior to operation, and in two of the infants progression of the emphysema occurred. In each case there had been confusion about the diagnosis. Most frequently it was thought that the infant had a large pulmonary cyst. On other occasions, it was felt that atelectasis or pneumonitis was present in the compressed lobes and that the emphysema was compensatory. In one infant a diagnosis of massive collapse of the opposite lung was made. Two of the infants were bronchoscoped prior to operation. The only abnormality noted was a tendency for the bronchi to collapse during expiration. No attempt was made in these infants to decompress the emphysematous lobe by thoracentesis prior to operation. Such an attempt would appear to be inadvisable.

Aortic Commissurotomy.—Larzelere and Bailey review the etiology and pathogenesis of aortic stenosis and point out that just as mitral stenosis can be corrected by instrumental and/or digital means, so can a stenosed aortic orifice be opened. The presence of three cusps in the aortic valve would mechanically provide even more assurance that an unfavorable insufficiency would not result from commissurotomy. The present mode of treatment and the instrument that will accomplish safe and adequate aortic commissurotomy are described. The instrument is the Bailey aortic dilator, which is a triradiate parallel expanding mechanism, containing three flanged blades. It is used to part the fused aortic commissures. A transventricular approach is used; the instrument is passed into place over a previously inserted beaded guide wire. The authors present observations on 42 patients in whom aortic commissurotomy was done. This number included 25 patients with significant mitral stenosis; 23 mitral commissurotomies were performed. Two of the 23 underwent simultaneous mitral commissurorrhaphy (commissural suturing) for significant associated insufficiency. Also, in the three cases of aortic stenosis associated with a significant degree of mitral insufficiency, two commissurorrhaphies of the mitral valve were performed. In one case of aortic insufficiency associated with slight degrees of aortic stenosis and mitral insufficiency, an aortic commissurotomy and a transaortic Nylon graft tamponage of the aortic valve were performed, along with mitral valve exploration. There were seven deaths in the 42 cases. One death occurred in the 13 patients with isolated aortic stenosis and was due to ventricular fibrillation. There were three deaths in 19 patients who had both aortic and mitral stenosis, and in 17 in whom both mitral and aortic commissurotomies were done. One of these was due to bleeding from the ventricular surgical wound; one resulted from a massive pulmonary embolism due to thrombosis of the right auricular appendage; and one resulted from recurrent pulmonary edema following mitral insufficiency produced at surgery. In five cases of aortic stenosis, mitral stenosis, and mitral insufficiency (each lesion sig-

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nificant), there were two deaths. One of these occurred on the operating table and was due to a tear in the hemostatic ventricular purse-string suture. The other death, 28 days postoperatively, was due to reactivation of rheumatic infection with pericarditis, congestive failure, and perhaps some induced aortic insufficiency. In three cases of aortic stenosis and mitral insufficiency (three aortic commissurotomies and two mitral commissurorrhaphies), there was one death caused by pulmonary edema probably resulting from a too tightly sutured mitral valve. The authors hope that aortic commissurotomy for aortic stenosis will prove to be as beneficial as mitral commissurotomy for mitral stenosis.

Journal of Urology, Baltimore

70:1-128 (July) 1953. **Partial Index**

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Clinical Diagnosis of Tumors of Adult Renal Parenchyma. E. Burns. —p. 9.
Renal Angiography. M. Harvard.—p. 15.
Ruptured Intrarenal Aneurysm. W. J. Baker and N. I. Huckleberry. —p. 20.
Perinephric Abscess with Perinephro-Bronchial Fistula: Case Report. L. R. Wharton Jr.—p. 26.
Peri-Ureteropelvic Cyst. J. Hyman.—p. 32.
Peri-Ureteritis Plastica: Report of Four Cases. S. A. Vest and B. Barelare Jr.—p. 38.
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Physiology of Uretero-Intestinal Anastomosis: II. Inhibitory Effect of Cortisone on Stricture Formation. R. Baker, D. Govan, J. Huffer and J. Cason.—p. 58.
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Observations on Normal and Abnormal Bladder Physiology. J. Lapides. —p. 74.
Malacoplakia of Urinary Tract: Report of Three Cases. W. H. Bennett. —p. 84.
Vaginal Transillumination in Suprapubic Repair of Vesicovaginal Fistula. E. C. Shaw.—p. 91.
Vesical Neck Obstructions in Children. H. P. McDonald, W. E. Upchurch and C. E. Sturdevant.—p. 94.
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"Adenomatoid" Tumor of Tunica Vaginalis. S. S. Ambrose Jr.—p. 110.
Furadantin in Infections of Genito-Urinary Tract. C. M. Norfleet Jr., P. R. Beamer and H. M. Carpenter.—p. 113.

Kansas Medical Society Journal, Topeka

54:249-312 (June) 1953

Poliomyelitis—Selective Five-Year Review. H. O. Marsh and C. D. Hensley Jr.—p. 249.
Renal Lithiasis and Recent Concepts in Treatment. C. A. Wattenberg and J. B. Beare.—p. 256.
Procedure for Repeated Infant Transfusion. F. A. Allen and A. G. Dietrich.—p. 263.
Pituitrin Induced Shock—Case Report. M. D. Atwood and H. Benvenuti. —p. 266.

54:313-360 (July) 1953

The Practitioner, the Surgeon and Acute Abdominal Disease. R. L. Sanders.—p. 313.
Iliac Bone Used as Barrel Stave Grafts for Non-Unions: Report of 81 Cases. H. O. Anderson.—p. 316.
Ketosteroids in Coronary Heart Disease. R. R. Howard and M. M. Gertler.—p. 319.
Indications for Pulmonary Resection. A. M. Tocker.—p. 323.

Missouri Medicine, St. Louis

50:579-656 (Aug.) 1953.

Injuries to Tarsus Bones. R. L. Diveley and R. H. Kiene.—p. 595.
Clinical Experiences with New Medium (70 Per Cent Urokon—Sodium) in Intravenous Urography. J. E. Byrne and W. F. Melick.—p. 599.
*Use of Hydrocortisone (Compound) by Local Injection in Arthritis and Allied Conditions. R. H. Ramsey and J. A. Key.—p. 604.
Trichlorethylene Analgesia and Anesthesia in Obstetrics and Minor Surgery. S. Brown and B. F. Fehlman.—p. 609.

Hydrocortisone (Compound F) by Local Injection in Arthritis.—Ramsey and Key present their observations on 119 patients with arthritis who received a total of 218 local injections of hydrocortisone. These patients had not received adrenal steroids by any other route, and they were observed for a sufficient period of time to permit evaluation of the results. The injections were given after 1% procaine had been injected into the skin and along the path of the needle but not into the joint, if this could be avoided. The hydrocortisone was then injected into the joint with another needle and syringe. The dose of hydrocortisone was from 25 to 50 mg. for the major joints and 5 to 20 mg. for the smaller joints. A total of 100 injections was given into 57 joints of 51 patients with hypertrophic arthritis. The response was considered satisfactory if there was at least a 50% relief in symptoms for a minimum of a week. With this criterion, 48 of 57 joints showed a satisfactory response. Many of these patients experienced nearly complete relief of symptoms for from 3 to 10 weeks or longer. In 14 patients with active rheumatoid arthritis 20 of 22 involved joints showed some response to intra-articular injections of hydrocortisone, but in general the response in these patients was of shorter duration than was the case in patients with hypertrophic arthritis. Thirty-three patients were given a total of 52 injections into painful bursas, with curative effect in 17 (mostly acute calcific bursitis of shoulder), partial relief in 9, and no benefit in 7. Tennis elbow, painful heels, acutely inflamed bunions and hemarthrosis of the knee following meniscectomy were some of the other conditions in which hydrocortisone was administered by local injection. No serious complications were observed in these patients, but the possibility of producing a septic arthritis by contamination should be kept in mind, and a careful injection technique should be used. The authors resorted to intra-articular injection only in selected cases with relatively severe symptoms, because they feel that a needle should not be introduced into a joint without good reason. While the treatment is not a panacea, it is a valuable therapeutic agent not only for acutely painful arthritic joints but also for its local anti-inflammatory action in several other painful conditions in which the etiology is obscure.

New England Journal of Medicine, Boston

249:45-84 (July 9) 1953

*Progressive Systemic Sclerosis (Scleroderma). P. M. Beigelman, F. Goldner Jr. and T. B. Bayles.—p. 45.
Family Outbreaks of Infectious Hepatitis: Prophylactic Use of Gamma Globulin. B. F. Brooks, D. Yi-Yung Hsia and S. S. Gellis.—p. 58.
Guillain-Barré Syndrome Associated with Acute Hepatitis. I. C. Plough and R. S. Ayerle.—p. 61.
Pediatric Radiology. E. B. D. Neuhauser and M. H. Wittenborg.—p. 62.
Evaluation of Tubeless Gastric Analysis: Report of 90 Determinations by Intubation and Tubeless Methods Made Simultaneously. F. P. Becker and M. Maslon.—p. 68.

249:85-124 (July 16) 1953

Management of Essential Hypertension. G. G. Duncan and R. J. Gill. —p. 85.
Idiopathic Ulcerative Colitis Beginning After Age of 50. B. M. Banks and M. I. Klayman.—p. 91.
Inhibition of Experimental Cholesterol Arteriosclerosis by Ultraviolet Irradiation. R. Altschul.—p. 96.
Postoperative Thrombophilia. R. Warren.—p. 99.

249:125-170 (July 23) 1953

Current Research Toward Global Control of Malaria. G. Covell.—p. 125.
Evaluation of New Antitussive Agent. L. J. Cass and W. S. Frederik. —p. 132.
Acute Pericarditis Associated with Infectious Mononucleosis. H. Miller, J. F. Uricchio and R. W. Phillips.—p. 136.
Use of New Oral Diuretic, Diamox, in Congestive Heart Failure. H. Belsky.—p. 140.
Management of Acute Glomerulonephritis. H. A. Derow.—p. 144.

Progressive Systemic Sclerosis (Scleroderma).—Beigelman and associates present observations on 15 patients with scleroderma, and suggest that the term progressive systemic sclerosis more accurately reflects the diffuse nature of the disease, which is not limited to the skin. Constitutional symptoms were present in all of the 15 cases. Twelve had lost weight, about half of the patients had noticed weakness or increased fatigability, and 6 had elevated temperatures. Twelve patients had typical Raynaud's syndrome. Joint pains or swelling or stiffness, or all three were present in 12 patients at some time during the course of their illness. Fourteen patients had cardiorespiratory embarrassment. Nine complained of dyspnea, and seven had ankle edema. Six patients had palpitations. Three were hoarse, without laryngeal infection. Eleven had complaints referable to the gastrointestinal system. Eight noted dysphagia. The earliest symptom in seven cases was referable to the joints rather than the skin. Of those who had skin manifestations

as the first sign of disease some noted thickening of the skin first, whereas others had pruritus, erythema, vitiligo and, in one case, felons. Roentgenograms were studied in nine cases. Common findings included pulmonary fibrotic streaks and nodules, cardiac changes, and esophageal abnormalities. Soft-tissue, bone, and joint lesions were frequent. Four patients had calcinosis. Electrocardiographic changes were frequent and arrhythmias were the most prominent. All autopsied cases demonstrated diffuse visceral fibrotic lesions. Vascular sclerosis and intimal hyperplasia were common. One case displayed inflammation of the mitral and tricuspid valves. All forms of therapy, including corticotropin and cortisone in most cases, proved ineffective. The histological findings in the present series, which confirm primary and basic involvement of connective tissue, place this disease, pathogenetically, in the same group with the collagen diseases, particularly disseminated lupus erythematosus. The major difference in the clinical picture and course of the two diseases can be perhaps explained through differences in the intensity and diffuseness of the reaction. Acute disseminated lupus suggests a comparatively severe, rapid connective tissue reaction, with edema and necrosis predominating, and progressive systemic sclerosis (scleroderma) represents a slow, torpid, generalized mesenchymal response, with fibrosis and sclerosis predominating. The ubiquitous proliferative hyaline vascular lesions observed in this series were probably sequelae of early, mild vessel-wall reaction preceding mesenchymal involvement.

New York State Journal of Medicine, New York

53:1601-1710 (July 15) 1953

Present Status of X-Ray Therapy in Neoplastic Diseases. E. P. Pendergrass.—p. 1643.
Palliative Treatment of Nonresectable Pulmonary Neoplasms—Primary and Metastatic. E. Mayer and B. Roswit.—p. 1647.
Pigmented Nevi: Their Relationship to Malignant Melanoma and Treatment. G. M. Lewis.—p. 1654.
Analysis of Cancer in Infancy and Childhood. J. E. Franklin.—p. 1659.
Treatment of Rheumatoid Arthritis. L. M. Lockie.—p. 1665.
Current Status of Medical Management of Pulmonary Tuberculosis. E. O. Coates Jr.—p. 1667.
Physical Medicine and Rehabilitation in Home Care Programs. D. A. Covalt.—p. 1671.
Hay Fever, Humidity, and Sinusitis: Further Studies. M. Unger.—p. 1674.
Preoperative Localization of Intervertebral Disk Hernias and Other Cord-Compressing Lesions. J. H. Siris.—p. 1677.
Eosinophilia. A. M. Fuchs.—p. 1681.
Femoral Hernia with an Analysis of 203 Cases. H. L. Skinner, G. W. Bolin and G. M. Gordon.—p. 1685.

Northwest Medicine, Seattle

52:605-696 (Aug.) 1953

*Report of 17 Cases Subjected to Intracardiac Exploration for Mitral Commissurotomy. K. A. Merendino, R. A. Bruce, D. L. Rodgers and J. W. Finley.—p. 625.
Recurrent and Overlooked Common Duct Calculi. M. F. Fuller.—p. 630.
Melanomas. J. L. Norris.—p. 633.
Office Diagnosis of Operable Congenital Heart Lesions. R. Tidwell, R. Rushmer and R. Polley.—p. 635.
Current Status of Acute Rheumatic Fever in State of Washington. R. A. Bruce.—p. 636.

Mitral Commissurotomy.—Merendino and co-workers select patients for commissurotomy on the basis of the physical fitness index, which is derived from performance while walking on a treadmill at 1.7 miles per hour on a 10% grade for 10 minutes. The patient is not permitted to walk either faster or slower; he must either walk or stop. Endurance is measured by the number of minutes he is able to walk. Information is obtained simultaneously by means of a face mask connected to a Beckman oxygen analyzer, which continuously records the amount of oxygen extracted from the atmosphere. The third factor utilized in computation of the physical fitness index is the total number of heart beats in the first three minutes following the termination of exercise, regardless of its duration. The formula of the physical fitness index is given. Commissurotomy was regarded as indicated: (1) in patients with mitral stenosis without serious left ventricular enlargement who are disabled by the disease; (2) in women with mitral stenosis in the childbearing age who have had heart failure with a previous pregnancy; and (3) in patients with rheumatic heart disease and left auricular enlargement who have exhibited one or more episodes of peripheral embolism. Fifteen patients with disabling mitral stenosis were operated on. An additional patient, a girl of 19, who was in severe cardiac failure during her last pregnancy, was subjected to prophylactic mitral commissurotomy, although following pregnancy she was not disabled in any way. In another patient, the mitral valve was explored; because of serious mitral regurgitation and the feeling of the surgeon that the patient would be harmed by commissurotomy, only ablation of the auricular appendage was carried out. No deaths occurred in these 17 patients, and there was no evidence of embolism during surgery. Of eight patients with fibrillation preoperatively, most had a trial period of quinidine therapy. In only three patients in this group was a normal sinus rhythm obtained after surgery. Quinidine is still necessary to maintain normal sinus rhythm. Two patients who received digitalis for years discontinued all cardiac medication. Almost two months must elapse before objective evidence of improvement can be noted. Those followed the longest have shown the best results. Improvement has been noted to continue for one year. Many patients who felt better postoperatively did not show objective improvement. Some who felt little different revealed an impressive improvement in their physical fitness index. It is of interest that those who felt considerably better following commissurotomy but who did not show early improvement in their physical fitness index subsequently improved. One important indication of the surgical result, which most patients note immediately, is improvement in their ability to breathe or take a deep breath.

Pediatrics, Springfield, Ill.

12:1-98 (July) 1953

Congenital Megacolon. O. Swenson.—p. 1.
Parahemophilia (Owren's Disease). B. Redner, H. Scalettar and M. Weiner.—p. 5.
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Behavior Changes Indicating Emotional Trauma in Tonsillectomized Children: Final Report. K. Jackson, R. Winkley, O. A. Faust and others.—p. 23.
Effects of Hydrazinophthalazine (Apresoline®) on Blood Pressure and Renal Function in Children with Acute Nephritis. W. W. McCrory and M. Rapoport.—p. 29.
*Chemotherapy of Miliary Tuberculosis and Tuberculous Meningitis. Public Health Service Cooperative Investigation.—p. 38.
Peptic Ulcer in Childhood. B. R. Girdany.—p. 56.
Adrenal Function in Premature Infants: II. ACTH-Treated Infants and Infant Born of Toxemic Mothers. J. T. Lanman.—p. 62.
ACTH in Treatment of Erythroblastosis: II. Progress Report. L. J. Geppert, J. H. Akeroyd and J. W. Simpson.—p. 72.

Chemotherapy of Miliary Tuberculosis and Tuberculous Meningitis.—The United States Public Health Service early in 1948 initiated a study of the use of Promizole (2-amino-5-sulfanilylthiazole) and *p*-aminosalicylic acid in combination with streptomycin for childhood miliary and meningeal tuberculosis. Two combinations of drugs were compared in a cooperative study of 32 children with acute hematogenous miliary tuberculosis treated at seven different pediatric centers under a common protocol. Eighteen children were given streptomycin intramuscularly and *p*-aminosalicylic acid and Promizole orally; 14 children were given streptomycin and *p*-aminosalicylic acid without Promizole. A one year follow-up of this small group showed no significant differences in the results from the use of Promizole. Five of 10 children treated initially with a streptomycin dose of 20 mg. per kilogram intramuscularly twice a day were either dead or had meningitis, while only 2 of 22 children treated with a 50 mg. dose died; one of these had meningitis. Twenty-six of the original 32 patients were alive 12 months after the start of treatment. Relapse of miliary disease was not encountered during the first year of this study. The optimum duration of treatment is still uncertain. The fact that three patients developed meningitis at 110, 125, and 130 days of study suggests that treatment should be relatively long. Another follow-up study, after a span of two to four years from the first day of treatment, revealed that all 26 patients were still alive. Twenty of the 24 children who had been in good condition without gross handicap or residual effects at the end of one year remained well. None of these had sequelae or relapses. The other six children, although free of miliary disease, had or were sus-

pected of having other forms of tuberculosis. Of 93 children with tuberculous meningitis, of whom 23 also had miliary tuberculosis, half were given streptomycin intramuscularly, streptomycin intrathecally, and *p*-aminosalicylic acid and Promizole by mouth. The remainder received an identical regimen except that Promizole was omitted. Forty-two patients survived the first year; 24 of these had no serious sequelae from the disease. No differences were noted in the course of the disease among those who received Promizole and those who did not, and the one year survival rates in the two groups were practically identical. Revision of the streptomycin dosage, which took place after the study had been in progress seven months, produced results that appear to justify the change. A dose of streptomycin of 50 mg. per kilogram intramuscularly twice daily to a maximum of 1.5 gm. twice daily was apparently more effective than 20 mg. per kilogram twice daily. From two to four years after onset of treatment 54 of the 93 children with tuberculous meningitis had died, 12 were living with gross residual effects, one patient could not be traced, and 26 were alive without significant sequelae from meningitis.

Psychosomatic Medicine, New York

15:279-320 (July-Aug.) 1953

Psychotic Reactions Induced by Corticotropin (ACTH) and Cortisone. G. H. Glaser.—p. 280.
Studies on Physiology of Awareness: Interrelationships of Emotions, Life Situations, and Anoxemia in Patients with Bronchial Asthma. J. W. L. Doust and D. Leigh.—p. 292.
Emotions and Hydrochloride Acid Secretion During Psychoanalytic Hours. G. F. Mahl and R. Karpe.—p. 312.
Development of New Symptoms Following Medical and Surgical Treatment for Duodenal Ulcer. J. S. Browning and J. H. Houseworth.—p. 328.
Electroencephalographic and Psychological Studies of Case of Migraine with Severe Preheadache Phenomena, with Comments on Cerebral Vasospasm and Focal Hypertensive Encephalopathy. G. L. Engel, W. W. Hamburger, M. Reiser and J. Plunkett.—p. 337.
Age and Sex in Eye Injuries of Children. T. F. Schlaegel Jr. and P. F. D. Seitz.—p. 349.

Public Health Reports, Washington, D. C.

68:737-828 (Aug.) 1953. **Partial Index**

Nutrition Research: Potentialities in Chronic Disease. W. H. Sebrell Jr.—p. 737.
Enrichment: Public Health Approach to Better Nutrition. W. H. Sebrell Jr.—p. 741.
*Agglutination of Treponema Pallidum in Syphilitic Serums. C. P. McLeod and H. J. Magnuson.—p. 747.
Sex Differences in Trend of Mortality from Certain Chronic Diseases. G. Kaufman and T. D. Woolsey.—p. 761.
Public Health Today—Nation's Best Investment. L. A. Scheele.—p. 771.
Half Century of International Control of Venereal Diseases. T. J. Bauer.—p. 779.
Incidence of Reactions to Antirabies Horse Serum. T. S. Hosty and F. R. Hunter.—p. 789.
Investigation of Jute Imports as Potential Plague Source. E. W. Norris, L. B. Schneider, L. J. Hanchett and others.—p. 802.

Agglutination of Treponema Pallidum in Syphilitic Serums.—Numerous unsuccessful attempts have been made to demonstrate specific agglutination of pathogenic Treponema pallidum in syphilitic serum. Most such attempts have met with failure because of the tendency of the organisms to agglutinate spontaneously. Interest in the subject was revived by the report of Tani that spirochetes killed with antiformin showed no such spontaneous clumping but were agglutinated in syphilitic serum after an incubation period of 24 hours, and that organisms so treated provided satisfactory antigens for the serodiagnosis of syphilis. The agglutination technique described was devised by bringing together the findings of two separate lines of investigation. The experiments of Tani were confirmed and extended. At the same time, there was in progress a study of complement in the Treponema pallidum immobilization test. A study was made of the effects of adding fresh steer serum to mixtures of T. pallidum and syphilitic serum. Because of its content of conglutinin, the steer serum caused disappearance rather than immobilization of the spirochetes under the conditions of the T. pallidum immobilization test and greatly accelerated and enhanced the clumping of the organisms in the agglutination test. The agglutination test performed by this method appears to compare favorably both in specificity and sensitivity with the T. pallidum immobilization test.

Radiology, Syracuse, N. Y.

61:1-160 (July) 1953

*Supraclavicular Shadows in Chest Film Interpretation. H. I. Amory and P. E. Sieber.—p. 8.
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Peptic Ulcers in Children, with Report of Four Cases. R. C. Aye.—p. 32.
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Calcification of Left Auricle. S. D. Hemley, A. Schwinger and L. A. Harrington.—p. 49.
Bilateral Aneurysms of Subclavian and Axillary Arteries: Report of Case. S. P. Perry and C. W. Massey.—p. 53.
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Congenital Hereditary Cranium Bifidum Occultum Frontalis, with Review of Anatomical Variations in Lower Midsagittal Region of Frontal Bones. R. J. Terrafranca and A. Zellis.—p. 60.
Symptomatic Hepato-Diaphragmatic Interposition of Colon. H. L. Hunter and R. Rapp.—p. 67.
Simple Device for Saving Films in Radiography of Intestine. S. Fineman.—p. 71.
Rapid Film-Changing Device for General Radiography: Preliminary Report. L. G. Rigler and J. C. Watson.—p. 77.
Device to Support Patients During Upright Fluoroscopic Examinations. H. L. Steinbach and L. B. Lusted.—p. 80.
Observations of Scattered Radiation Inside and Outside a 1,000-Curie Cobalt ™ Teletherapy Room. J. G. Brown.—p. 82.
Thyroid Gland Weight Determination from Thyroid Scintigrams with Postmortem Verification. W. E. Goodwin, B. Cassen and F. K. Bauer.—p. 88.
The n Unit and Energy Absorption in Tissue. H. H. Rossi.—p. 93.
Effects of Acute Whole-Body X-Irradiation on Salt and Water Metabolism and Their Clinical Significance. J. Z. Bowers, V. Davenport, N. Christensen and C. J. Goodner.—p. 97.
X-Ray Absorption Coefficients for Borosilicate Glass. S. L. Whitcher and N. Todd.—p. 103.

Supraclavicular Shadows in Chest Films.—Supraclavicular shadows, present on most posteroanterior films of the chest, are pointed out as normal features, and the student is cautioned against confusing them with pathological lesions. Masses in the neck resulting from lymphomas, tuberculosis, thyroid, salivary gland, laryngeal, and superior sulcus tumors, and metastatic involvement from carcinoma of the breast and testes may partially or completely obliterate the supraclavicular fossas, either as a result of metastasis from a distant primary lesion or by direct extension. Thus tumors or other disease processes that result in obliteration of the supraclavicular fossas can be detected roentgenographically by absence of one or both of the supraclavicular shadows. Twelve cases showing abnormal supraclavicular shadows produced by disease are presented and several are illustrated. An evaluation of supraclavicular shadows should be made routinely during the interpretation of all posteroanterior films of the chest. If the shadows are present bilaterally and are normal in appearance, no comment should be made concerning them. Unilateral absence should be reported and investigated clinically, provided the film does not indicate obesity or gross malposition. Bilateral absence may be significant and should be investigated when the patient is of normal or subnormal weight.

Science, Washington, D. C.

118:1-32 (July 3) 1953. **Partial Index**

Susceptibility of Starch in Fresh and Stale Bread to Enzymatic Digestion. S. S. Jackel, A. S. Schultz and W. E. Schaeder.—p. 18.
*Estrogen Excretion in Women with Mammary Cancer Before and After Adrenalectomy. T. L-Y. Dao.—p. 21.
Hydrogen Ion Concentration of Human Fetal Blood in Utero at Term. I. H. Kaiser.—p. 29.

Estrogen Excretion in Women with Breast Cancer Before and After Adrenalectomy.—Estrogen assays were performed on the urine of 12 women with breast cancer and of 12 normal women who served as controls. The urinary excretion of estrogen in premenopausal women was in the same range regardless of the presence or absence of breast cancer. Elimination of ovarian function by roentgen irradiation or ovariectomy led to lowered values of estrogen in the urine. When adrenalectomy was performed after elimination of ovarian function, estrogen was no longer detectable in the urine. Nine

of 12 patients with mammary cancer subjected to adrenalectomy showed a measurable decrease in the neoplastic involvement after the operation. The author stresses that patients with breast cancer who had had eradication of ovarian function by irradiation or surgical excision still excreted estrogen in significant amount; that adrenalectomy eliminated estrogen from the urine of those cases. It is evident that the adrenals are the only significant source of estrogen in women with breast cancer who do not have active ovarian function. The three patients with mammary cancer who did not have a regression of the neoplasm after adrenalectomy, excreted preoperatively amounts of estrogen, which in two cases were below the mean titer for ovariectomized women. It is not possible to state from this study that the reduction of estrogen was the critical factor in the remission of the disease in the patients who were benefited.

South Carolina Medical Assn. Journal, Florence

49:171-198 (July) 1953

Urological Problems in the Female. R. Lich Jr.—p. 171.
True Hermaphroditism with Report of Case. W. C. Cantey.—p. 175.
Arteriosclerosis. E. W. Masters.—p. 181.

Southern Medical Journal, Birmingham, Ala.

46:633-728 (July) 1953

Surgical Treatment of Malignant Tumors of Eyelid. L. Turner and S. D. McPherson Jr.—p. 633.
Correction of Funnel Chest Deformity. J. C. Chesney and D. C. Daughtry.—p. 636.
The Midwife, Should She be Ignored, Eliminated or Controlled? E. F. Dodge, W. E. Brown and F. Rothert.—p. 639.
Management of Psychiatric Patients with Abnormal Electroencephalograms. I. Pine and M. M. Parker.—p. 645.
Electrodynamic Field Theory in Psychiatry. L. J. Ravitz.—p. 650.
Carcinoma of Pancreas: Comparison of Clinical and Laboratory Findings of Carcinoma of Pancreas and Chronic Pancreatitis. W. A. Knight Jr. and R. O. Muether.—p. 660.
Knee Trauma. E. Margo.—p. 667.
Rectal Paraldehyde: Basal Anesthetic for Children. S. H. Axelrod and C. Stein.—p. 670.
Proctology Twenty Years Ago and Now. J. Cheleden.—p. 673.
Anoplasty Versus Hemorrhoidectomy. M. M. Marks.—p. 678.
Present Day Concepts and Uses of Vaginal Hysterectomy. C. S. McMurray.—p. 680.
Modified Suprapubic Prostatectomy. E. W. Brown.—p. 689.
Bladder Neck Obstruction in Females. W. A. Van Nortwick, R. B. McIver and R. J. Brown.—p. 691.
Program of Tuberculosis Control in Recent Years. C. M. Sharp.—p. 695.
*After-Cough Fainting as Complication of Bronchial Asthma. V. J. Derbes and A. Kerr Jr.—p. 701.
Present Day Status of Infectious Eczematoid Dermatitis. C. B. Kennedy, V. M. Henington and W. H. Garvin.—p. 707.
Treatment of Chronic Middle Ear Including Anterior Myringotomy in Secretory Otitis Media and Pathogenesis of Cholesteatoma. R. A. Bagby and J. B. Farrior.—p. 712.
Left Recurrent Laryngeal Nerve Paralysis in Patient with Arteriosclerotic Heart Disease. A. B. Tashnek.—p. 718.
Duane Retraction Syndrome: Strabismus Problem. R. H. Myers.—p. 720.

After-Cough Fainting in Bronchial Asthma.—According to Derbes and Kerr, few physicians are aware that fainting after coughing is frequently a complication of bronchial asthma. Although the condition is not frequent, failure to recognize this syndrome in asthmatic patients leads to confusion, needless consultation, and undue apprehension. The syndrome of syncope following cough has been reported under such terms as laryngeal vertigo, laryngeal ictus, laryngeal apoplexy, bronchial syncope, cough syndrome, tussive syncope, posttussive syncope, and tussigenic ictus. The condition is much more frequent in men than in women, all but 9 of the 290 cases, so far reported, involving men. The authors observed 35 cases of this complication, which they described previously. The illustrative case presented here was that of a 30-year-old physician. Chest examination often discloses chronic infection. Of the authors' patients, 9 had asthma, 12 emphysema, 3 bronchiectasis, 2 pneumonoconiosis, and 1 sarcoidosis. Of 28 patients questioned regarding the use of alcohol, only 2 were abstainers. The cough is usually dry, barking, paroxysmal, and obstinate. It may be accompanied by dyspnea, congestion or asphyxia. The face is congested during the attack, and is either red or cyanotic. Although the syndrome is usually self-limited and benign, the course varies greatly. Four deaths have been reported from after-cough fainting. The attack itself requires little treatment, because it terminates quickly as a rule. Some patients who experience premonitory symptoms feel that they can abort an attack by measures such as firmly grasping an object for support, holding the breath, grasping the larynx, sucking a lozenge, spraying coccaine in the pharynx, or fanning themselves. Certain other patients having warning symptoms, but not being able to abort the attack, can place themselves in a position to minimize harming themselves in the anticipated fall. In cases associated with bronchial asthma the treatment of after-cough syncope consists of intensive treatment of the bronchial asthma.

Surgery, St. Louis

34:169-336 (Aug.) 1953

Observations on Liberation and Elimination of Myohemoglobin and of Hemoglobin After Release of Muscle Ischemia. C. A. Montagnani and F. A. Simeone.—p. 169.
Prevention of Carotid Artery Hemorrhage by Use of Rotating Tissue Flaps. J. J. Conley.—p. 186.
Experimental Cardiac Surgery: IV. Prevention of Air Embolism in Open Heart Surgery; Repair of Interauricular Septal Defects. W. W. L. Glenn and W. H. Sewell Jr.—p. 195.
Some Effects upon Liver of Complete Arterialization of Its Blood Supply: III. Acute Vascular Necrosis. L. J. Rather and J. Cohn.—p. 207.
Factors Contributing to Renal Enlargement After Ureterodouodenostomy and Contralateral Nephrectomy. M. A. Block, K. G. Wakim, J. H. Grindlay and F. C. Mann.—p. 211.
*An Evaluation of Segmental Gastric Resection for Treatment of Peptic Ulcer. L. D. McLean, W. Hamilton and T. O. Murphy.—p. 227.
Use of Preserved Bile Duct Homografts to Bridge Common Duct Defects: Experimental Study. H. J. Leary, G. E. Kelley and W. J. Michaels Jr.—p. 238.
Problems in Management of Anterior Chest Wall Tumors. J. E. Macmanus, R. C. McCormick and M. P. Fecher.—p. 245.
Side-to-Side Intestinal Anastomosis Complicated by Ulceration, Dilatation, and Anemia: Physiologically Unsound Procedure; Review of Literature and Presentation of Case. D. K. Clawson.—p. 254.
Benign and Malignant (Sarcoma) Stromal Endometriosus: 11 Year Progress Report of Previously Reported Cases; 10 New Examples, Including One Followed for 24 Years. W. C. Hunter.—p. 258.
Surgical Method of Treatment of Carcinoma of Floor of Mouth. D. B. Greer, R. R. Smith and C. T. Klopp.—p. 279.
High Cervical Chordotomy: Preliminary Report. G. E. Roulhac.—p. 288.
Thrombophlebitis with Ischemia and Gangrene. C. D. Hershey and R. E. Snyder.—p. 296.
New Noncrushing Clamp with Universal Joint for Blood Vessel Surgery. R. S. Gilfillan, T. Masuda, E. D. Green and N. E. Freeman.—p. 303.
External Laryngocele. J. H. Johnston Jr.—p. 307.

Segmental Gastric Resection for Treatment of Peptic Ulcer.—MacLean and associates present a critical evaluation of segmental gastric resections as performed at the hospital of the University of Minnesota during the last two and one-half years. The results obtained in 90 patients treated with this method were compared with those in 953 patients, who earlier underwent Billroth 2 type gastric resections between the years of 1940 and 1949 for benign lesions of the esophagus, stomach, or duodenum. It was found that segmental gastric resection in which all but 10 to 15% of the acid-secreting area of the stomach is resected is a satisfactory operation for peptic ulcer when accompanied by pyloroplasty. Not only benign gastric and duodenal ulcer, but also esophagitis and lower esophageal stricture were treated successfully with segmental resection. In the presence of supraduodenal ulceration or a scarred and deformed duodenum, the difficulties of closure or anastomosis in this area can be avoided by utilizing segmental resection. Postprandial distress occurs early after segmental resection, but anemia and recurrent ulceration were never observed in the careful follow-up of 90 patients. Food intolerance was limited to milk, ice cream and sweets, but this was frequently encountered. Eighty-eight per cent of the patients lost weight compared to their weight five years before operation. The average weight loss was 19 lb. (8.6 kg.). Over 90% of the patients felt they were improved or greatly improved by

the operation. Four patients felt they had not been helped. On the basis of technical advantages, physiological aspects, and careful postoperative evaluation, the authors consider segmental gastric resection a superior operation for the acid peptic diathesis to the Billroth 2 procedure.

Surgery, Gynecology and Obstetrics, Chicago

97:129-256 (Aug.) 1953

Limitations of Radical Surgery in Treatment of Cancer. H. B. Stone. —p. 129.
Primary Tumors of Duodenum. R. E. Ebert, G. F. Parkhurst, O. A. Melendy and M. P. Osborne.—p. 135.
Relief of Postthoracotomy Pain. W. R. Deaton Jr. and H. H. Bradshaw. —p. 140.
Deposition of Radiophosphorus in Fractured Bones in Rats. G. W. Wilkinson and C. P. Leblond.—p. 143.
*Radical Gastrectomy for Benign Gastric Ulcer. A. M. Boyden.—p. 151.
Bone Changes Following Bilateral Ureterosigmoidostomy. M. S. Sherman. —p. 159.
Electrolyte Changes in Healing Muscle Wounds in Dog. J. A. Schilling, A. B. McCoord, S. W. Clausen and others.—p. 162.
Acute Cholecystitis Following Operation for Unrelated Disease. C. W. Schwegman and W. E. De Muth Jr.—p. 167.
Blood Volume in Pregnancy as Determined by P^{32} Labeled Red Blood Cells. N. I. Berlin, C. Goetsch, G. M. Hyde and R. J. Parsons. —p. 173.
Multiple Organ Resection for Advanced Carcinoma of Colon and Rectum. J. Van Prohaska, M. C. Govostis and M. Wasick.—p. 177.
Fracture of Proximal Portion of Tibia in Children Followed by Valgus Deformity. L. Cozen.—p. 183.
Experimental Uremia: Excessive Quantities of Plasma Protein and Nitrogen Removed in Outflow Fluid During Peritoneal Irrigation of Bilaterally Nephrectomized Dogs. E. E. Muirhead, F. Jones, J. A. Stirman and W. Lesch.—p. 189.
War Wounds of Chest Among Marine and Naval Casualties in Korea. J. D. King and J. H. Harris.—p. 199.
Collateral Venous Drainage from Kidney Following Occlusion of Renal Vein in Dog. W. H. Hollinshead and J. A. McFarlane.—p. 213.
*Use of Streptokinase-Streptodornase in Treatment of Thoracic Empyema. J. J. Finnerty.—p. 220.
Cytologic Criteria of Gastric Cancer. F. G. Panico.—p. 233.

Radical Gastrectomy for Benign Gastric Ulcer.—The common surgical procedure for gastric ulcer, according to Boyden, is removal of the lower two-thirds of the stomach. For the ulcer proving to be malignant such an operation is entirely inadequate. Were it possible to determine at operation which gastric ulcers are malignant, then wide excision of the lymphatic bed could be performed in those cases. But with the stomach in his hand, the surgeon cannot tell the malignant from the benign ulcer, and it is usually no more apparent to the pathologist on gross examination. Biopsy of the ulcer margin may miss the area of malignancy. Excision of the ulcer for frozen section is commonly misleading because of the difficulty of accurate interpretation by this method in this organ. Excision of the ulcer for immediate examination is often impractical because of its location or adherence to adjacent organs. Biopsy of one or two lymph nodes is inadequate. The ideal treatment of carcinoma of the stomach is total gastrectomy with excision of wide segments of the duodenum and esophagus and removal of all of the greater and lesser omenta, the gastrocolic omentum, and the spleen. Admittedly a compromise, radical subtotal gastrectomy should include all of the zones of lymphatic spread. Boyden reviewed the records of all patients operated on at the Portland Clinic for gastric ulcer and carcinoma during the 6 years from 1946 to 1952. During this interval 70 patients with gastric ulcer were operated on. Pathological examinations were made in 66 cases (eliminating 3 cases of perforated ulcer and 1 of vagotomy and gastroenterostomy). Eight of these lesions were malignant. During the same period (1946 to 1952) 74 patients were operated on in the Portland Clinic for carcinoma of the stomach. These include the 8 with malignant ulcers mentioned previously. Twenty-four lesions were inoperable. Subtotal gastrectomy was undertaken in 38 cases, total gastrectomy in 8, partial esophagogastrectomy in 4. The operative mortality in all resections was 14%. The author advocates subtotal gastrectomy for all gastric ulcers.

Streptokinase-Streptodornase in Thoracic Empyema.—Finnerty reviews the evolution of the treatment of empyema and gives particular attention to the use of streptokinase-streptodornase, which, in addition to making the purulent exudate less viscous, accomplishes several other objectives: It breaks up loculations, converts the empyema space into a single one, and thus renders it more available to the action of locally instilled antibiotics. It also obviates the necessity of needle aspirations in multiple sites. Organisms trapped in the fibrin mesh are liberated and are more liable to the action of antibiotics. The fibrin peel on the pleural surfaces is lysed, thus enabling the lung to expand and obliterate the dead space. This debridement of the pleural surfaces probably also allows the antibiotic, as well as the patient's own leukocytes and antibodies, to enter the infected area and exert their effect. The streptokinase-streptodornase is supplied in moisture-proof sterile ampuls, each ampul containing approximately 100,000 units of streptokinase and about ¼ that amount of streptodornase. About 100,000 to 200,000 units of streptokinase are diluted in 30 to 40 cc. of sterile isotonic sodium chloride solution and are injected into the empyema space. From 8 to 18 hours later thoracentesis is performed. Many patients require only one or two treatments, but some require many. The most important point is that, after injection of the enzymes, complete aspiration must be done, because the enzyme action is self-terminating and, if the lysed material is not removed, redeposition of fibrin will occur. Most failures are due to inadequate removal of liquified material or to the enzymes not having been injected into the proper area in adequate dosages. Because of this and because of the fact that patients frequently object to multiple thoracentesis, it occurred to the author that the use of antibiotics and enzymes in combination with surgical closed intercostal drainage with active suction might represent a further advance in the therapy of empyemas. The obvious advantage of this method over that just described is that constant drainage should shorten the therapy and be more comfortable for the patient and less time consuming for the physician. Accordingly, 15 patients were treated by this method. The conditions included putrid empyemas, lung abscess with large bronchopleural fistulas, and Friedländer's abscess with fistula and empyema. The method obliterated the empyema spaces and rendered more suitable for surgery those in which excision was indicated. The plan of this treatment and several case histories are presented.

Virginia Medical Monthly, Richmond

80:417-476 (Aug.) 1953

Abuse of Bed Rest in Therapy of Cardiac Patients. N. F. Wyatt, J. R. Beckwith and J. E. Wood Jr.—p. 419.
Diagnosis and Treatment of Intestinal Obstruction. C. Williams.—p. 426.
Surgical Treatment of Inguinal Hernia in Infancy and Childhood—Changing Concepts. C. E. Davis Jr.—p. 431.
Simple Procedure Useful in Diagnosis and Treatment of Diseases of Chest. B. B. Jones.—p. 437.
Operative Procedure for Correction of Unshapely Detractive Nose. W. L. Gatewood.—p. 440.
Cancer Detection. G. Z. Williams.—p. 444.
Multilocular Cysts of Kidney with Malignant Changes. C. I. Sease Jr. —p. 447.
Weapon for Eradication of Pulmonary Tuberculosis—Routine Sputum Test by Local Medical Doctor. W. E. Roye and P. P. Powers.—p. 451.

West Virginia Medical Journal, Charleston

49:217-244 (Aug.) 1953

The Price of Glory. J. S. Klumpp.—p. 217.
Motion Sickness. E. J. Van Liere.—p. 222.
Irradiation Therapy as an Adjunct to Surgery. V. L. Peterson.—p. 225.
Involutional Melancholia. A. D. Weatherhead.—p. 227.
The Surgeon, the Psychiatrist and the Patient with Peptic Ulcer. W. B. Rossman.—p. 231.

FOREIGN

Archiv für klinische Chirurgie, Berlin

274:465-634 (Nos. 6 & 7) 1953. **Partial Index**

Problem of Warming During Postoperative Phase. M. Reifferscheid and K. Dietmann.—p. 465.
Clinical Aspects and Surgical Treatment of Tuberculosis of Brain and Meninges. F. Pampus.—p. 470.
Profuse Mucosal Hemorrhages of Neurovascular Origin: Clinical and Experimental Observations. W. Wachsmuth.—p. 490.
*Cobalt Isotope, Co^{60}, for Postoperative Irradiation of Bronchial Carcinoma. W. E. J. Schneidrzik, C. Winkler and A. Kuske.—p. 538.
Roentgenologic Demonstration of Stenosis of Aortic Isthmus. R. Janker.—p. 548.
Cardiac Arrest and Ventricular Fibrillation. K. Dietmann and A. Gütgemann.—p. 562.
Surgical Interventions on Hypophysis and Adrenals. K. H. Bauer.—p. 606.

Radioactive Cobalt in Postoperative Treatment of Bronchial Carcinoma.—Schneidrzik and associates use a solution of radioactive Cobalt (Co^{60}), which had proved effective in the treatment of bladder tumors. The relative harmlessness of this form of irradiation for the adjoining structures had been proved by experiments on dogs. The authors chose a Foley catheter as the most suitable container for the radioactive solution. The construction of the Foley catheter with its thick and thin tubes and rubber balloon is described. After pulmonary resection the catheter is placed into the thorax in such a manner that the balloon, which can be inflated to a capacity of about 35 cc., rests on the hilus. The catheter is secured by means of a thread above and below the balloon, which, when empty and collapsed, can be pulled out from beneath these securing sutures. Both tubes of the catheter are led outward through an intercostal space. On the ninth postoperative day about 35 cc. of radioactive cobalt solution is placed into the balloon through the small-caliber tube. The patient now has to be isolated so that others will not be damaged by the gamma radiation, readily detectable in the surroundings of the patient with the aid of a Geiger counter. The radioactive fluid is suctioned off from five to seven days later. The histories of three patients in whom this form of irradiation was employed after pneumonectomy are cited. This form of intrathoracic irradiation was comparatively simple, reduced the time required for irradiation, impaired the patient's general condition only slightly, and insured favorable distribution of the ray dosage.

Archivos Instituto Cardiologia de Mexico, Mexico, D.F.

23:131-278 (April 30) 1953. **Partial Index**

*Patent Ductus Arteriosus with Pulmonary Hypertension. I. Chávez, E. Cabrera and R. Limón.—p. 131.
Intracardiac Valvulotomy by Means of Catheter. V. Rubio-Alvarez, R. Limón L. and J. Soni.—p. 183.
Mitral Stenosis: Clinical, Physiological, and Surgical Aspects. L. Dexter.—p. 193.
Clinical Aspects of Bacterial Endocarditis (Especially Thermic Curve). S. Aceves and T. Cesarman.—p. 235.

Patent Ductus Arteriosus with Pulmonary Hypertension.—Observations were made on 40 patients, including 24 children of the ages of 3 and 11 years, 14 young adults, not older than 30 years, and 2 adults 54 and 65 years old. The diagnosis of the congenital abnormality was confirmed by passing the catheter into the ductus and into the thoracic aorta in 34 patients, and by operation in six. The patients were placed in three groups with regard to the degree of pulmonary hypertension: group 1 included those between 30 and 60 mm.; group 2, those with 61 and 100 mm.; and group 3, those with 100 and 136 mm. The clinical symptoms, roentgen signs, and the electrocardiogram in the 14 patients of the first group were typical of a patent ductus arteriosus. In the 14 patients in the second group and in 12 in the third the changes observed corresponded to the degree of hypertension. In the patients of the second group, the continuous typical murmur changed into a double systolic and diastolic murmur. Both the left ventricle and the right ventricle were enlarged and showed strain in the electrocardiogram. The shunt was from the aorta into the pulmonary artery. In 11 of the 12 patients in the third group the continuous murmur had disappeared and was replaced by a systolic murmur heard at the base of the heart. A diastolic rumbling murmur, resembling that of mitral stenosis, was heard in three patients. Both ventricles were greatly enlarged, but the enlargement of the right ventricle masked the enlargement of the left. The electrocardiogram showed marked strain of the right ventricle. In severe cases the flow of blood through the patent ductus became crossed and the patients showed a diffuse cyanosis, which was particularly intense in the lower half of the body. The clinical signs were uncertain. The diagnosis was arrived at by sounding the patent ductus. The severe type of pulmonary hypertension is more frequent in children than in adults, suggesting that the condition is primary and not the result of the shunt. Surgery may control hypertension or may prove ineffective. Diagnosis of the syndrome of a patent ductus arteriosus with pulmonary hypertension is possible without catheterization if the patient with a congenital heart disease, with or without cyanosis, presents a systolic murmur at the base of the heart, an electrocardiogram with right ventricular strain, in absence of a polyphasic QRS in the sixth lead, and a radiological picture of pulmonary hypertension with pulsation along the entire left cardiac border of the shadow, which sometimes reaches the hilar vascular shadows.

British Medical Journal, London

2:1-46 (July 4) 1953

The Doctor in the Witness-Box. V. Simon.—p. 1.
Early Complications of Cardiac Infarction. H. E. S. Pearson.—p. 4.
Diagnosis of Cardiac Infarction. R. S. Stevens.—p. 9.
*Familial Hypertrophic Pyloric Stenosis. T. Fenwick.—p. 12.
Post-Partum Venous Thrombosis and Leg Ulcers. S. T. Anning.—p. 14.
*Emergency Thoracotomy for Massive Spontaneous Haemopneumothorax. J. Borrie.—p. 16.
Manipulation and Accurate Manual Methods in General Practice. R. Barbor.—p. 18.
Diagnosis of Thyrotoxicosis by Simple Out-Patient Radioactive Iodine Technique. A. G. Macgregor, H. Miller, P. J. Blaney and W. S. Whimster.—p. 21.
Case of Primary Biliary Cirrhosis. H. G. H. Richards and C. B. S. Fuller.—p. 23.

Familial Hypertrophic Pyloric Stenosis.—In the family cited by Fenwick, hypertrophic pyloric stenosis was discovered at operation in a man, aged 39. He subsequently revealed that two of his four sons had had the Ramstedt operation (pyloromyotomy) performed upon them in infancy, and he had a nephew treated medically for this condition in infancy. In addition, his eldest brother died in infancy from persistent vomiting. The case histories of the man, his two sons, and his nephew (son of his sister) are presented. In this last case the trait passed through a female member of the family. The occurrence of pyloric stenosis in one adult and three children in this family supports the contention that the adult and infantile conditions are the same and that a familial incidence does exist. In the infant, the Ramstedt operation is accepted as the standard procedure. In the adult a variety of procedures have been adopted. They include Ramstedt's sphincterotomy, finger dilatation of the pylorus, plastic procedures on the pylorus, gastroenterostomy, and gastrectomy, either partial or subtotal. The object of surgical treatment is to relieve the obstruction, and this is best done by removing it altogether. The man, whose case is reported, had high normal acidity. A Billroth 1 partial gastrectomy was performed, approximately half the stomach being removed. The result is satisfactory. If the acidity is low, Billroth 1 pylorectomy as recommended by McCann and Dean would seem to be equally satisfactory in that the lesion is removed and a relatively large stomach remnant remains.

Emergency Thoracotomy in Spontaneous Hemothorax.—The purpose of this report is to emphasize the serious nature of spontaneous hemopneumothorax, to stress that its onset may be delayed after the onset of the accompanying spontaneous pneumothorax, and to report two cases with massive spontaneous pneumothorax, both of which were successfully treated by emergency thoracotomy. Evacuation of blood and blood clot from the pleural cavity, control of the bleeding-point, and immediate reexpansion of the totally collapsed lung, was followed by rapid recovery and return to normal

life. The third patient, seen three weeks after the onset of the hemopneumothorax, required decortication of his lung. A review of the literature disclosed that 19 of 91 previously reported cases were fatal. Only four patients, including the two reported here, have so far been treated by emergency thoracotomy. Massive spontaneous hemopneumothorax is a surgical emergency which is best treated by resuscitation of the patient, early emergency thoracotomy, evacuation of the blood and blood clot, control of the bleeding-point, treatment of the causative lesion, and the induction of an artificial pleurisy to prevent recurrence. With emergency thoracotomy recovery can be rapid and complete.

2:57-108 (July 11) 1953

Mechanical Heart-Lung for Use in Man. D. G. Melrose.—p. 57.
Experimental Physiology of Heart-Lung Machine in Parallel with Normal Circulation. D. G. Melrose, J. W. Bassett, P. Beaconsfield and others.—p. 62.
Post-Inoculation Poliomyelitis. J. Grant.—p. 66.
Acute Appendicitis in Infancy and Early Childhood. G. L. Bunton.—p. 71.
Principles and Practice of Yaws Control. C. J. Hackett.—p. 74.
Effect of Large Doses of Histamine on Gastric Secretion of HCl: An Augmented Histamine Test. A. W. Kay.—p. 77.
An Antihistamine in Fenestration Operation for Otosclerosis. T. Cawthorne and P. B. Foxwell.—p. 80.
*A Human Blood-Group Chimera. I. Dunsford, C. C. Bowley, A. M. Hutchison and others.—p. 81.
Reactivation of Varicella Virus by Cortisone Therapy. J. C. Shee and P. Fehrsen.—p. 82.

A Blood Group Chimera.—Dunsford and collaborators report the case of a blood donor, a woman, aged 25, whose blood when grouped seemed to be a mixture of A and O cells, for anti-A serum caused large agglutinates to appear to the naked eye but the microscope showed these agglutinates to be set in a background of unagglutinated cells. The appearance was such as might be seen for a time after a large transfusion of O blood into an A recipient, but the woman had never received a transfusion. Further samples of her blood ruled out the possibility of accidental mixing of bloods. Observations on this woman's blood called to mind the work of Owen in 1945 on "immunogenetic consequences of vascular anastomoses between bovine twins." Anastomoses are usually present between bovine twin embryos; primordial red cells belonging to one twin take root in the other twin and continue throughout the life of that animal to produce red cells with genetically foreign antigens. Chorionic vascular anastomosis and transfer of endocrine secretions between bovine twins of different sex had been postulated as the cause of the freemartin condition by Lillie as early as 1916. When asked if she were a twin, the woman donor, somewhat surprised, answered that her twin brother had died 25 years ago at the age of 3 months. This woman is the first human being to be shown to have a double set of blood groups, and there can be little doubt that this is the consequence of vascular communication with her twin. Though hematologists have been prepared for this discovery by the work of Owen on bovine twins, such a mixture of blood cannot be common in human twins: the Blood Group Research Unit tested the blood of 58 pairs of dissimilar twins and 82 pairs of apparently identical twins without finding evidence of mixed blood groups.

Harefuah, Jerusalem-Tel Aviv

44:263-288 (June 15) 1953. **Partial Index**

*Terramycin in Treatment of Relapsing Fever. A. Gefel and R. Rubenow.—p. 263.
*Cancer of Breast and Its Occurrence in Israeli Women. H. Kook.—p. 266.
Pathology of Sleep. A. Stern.—p. 268.

Oxytetracycline (Terramycin) in Relapsing Fever.—The tick-borne type of relapsing fever, which is prevalent in Israel, is known to be resistant to arsenicals, penicillin, gold, and bismuth compounds. Gefel and Rubenow point out that experiments carried out by Adler and co-workers proved that oxytetracycline has a specific influence on rats inoculated with Spirochaeta persica. The authors themselves used oxytetracycline in the treatment of seven cases of relapsing fever. The drug was given orally to two, intravenously to four, and intramuscularly to one. A relapse occurred in one patient treated orally with 55.5 mg. per kilogram of body weight daily for five days. In all patients receiving parenteral treatment, the temperature dropped within 24 hours, clinical signs disappeared gradually, and the blood was cleared of parasites within a few hours, in one case within 45 minutes. The importance of the blood sedimentation rate in the prognosis of relapsing fever is emphasized. Relapses occurred in four cases of nonspecific treatment in which the sedimentation rate did not return to normal levels after the fall of the temperature. Acquired hemolytic anemia, due to the action of the spirochetes, developed in two of the patients; this complication has not been reported before.

Cancer of the Breast in Israeli Women.—A statistical study of cancer of the breast in Israeli women revealed that it occurs with a frequency about twice that given in the literature for other countries. During the years 1945-1947, 1,760 malignant tumors were found and 394 cases (22.3%) were of cancer of the breast. Only 9% of the women were of Oriental origin, while the proportion of these women in the whole population was 26% in the period under survey. Eleven per cent of the women were unmarried or married but sterile. The author believes that the increase of breast cancer is a result of late marriage and limited fertility. Where birth control is being practiced, it has been accompanied by an increase of mammary cancer. Figures of success rate in cancers of stage 1 and 2 are compared with results reported in the American literature. The somewhat higher success rates in Israel are attributed to the fact that Israeli women consult their physicians early.

Journal of Laryngology and Otology, London

67:377-436 (July) 1953

Surgery of Temporal Bone. T. Cawthorne.—p. 377.
Fenestration and Anatomo-Physiological Essentials for Its Success. C. A. Hutchinson.—p. 392.
Late Results of Treatment by Interstitial Irradiation of 100 Cases of Carcinoma of Bronchus. F. C. Ormerod.—p. 406.
Lingual Thyroid. H. W. Schwartz.—p. 417.

Lancet, London

2:1-48 (July 4) 1953

Viral Vaccines and Human Welfare. H. R. Cox.—p. 1.
Quantitative Assessment of Disability in Mitral Stenosis. J. P. P. Stock and M. C. S. Kennedy.—p. 5.
Is Scalp Ringworm in Children a Self-Limiting Disease? An Epidemic of Unusually Mild Form Produced by Microsporum Audouini, Dysgonic Type. C. H. Whittle.—p. 10.
Mechanism of Lowered Renal Threshold for Glucose in Diabetes. J. A. Robertson and C. H. Gray.—p. 12.
Renal-Function Tests in Renal Glycosuria Including Observations During Pregnancy. J. A. Robertson and C. H. Gray.—p. 15.
Resistance to d-Tubocurarine Chloride in Presence of Liver Damage. J. W. Dundee and T. C. Gray.—p. 16.
Idiopathic Hypercalcaemia of Infants. R. D. G. Creery.—p. 17.
Effects of Forceps Delivery on Child. H. R. MacLennan, A. B. Hay and M. L. Paterson.—p. 19.

2:49-98 (July 11) 1953

Prevention of Dust Diseases. A. I. G. McLaughlin.—p. 49.
*Folic-Acid Excretion Test in Investigation of Intestinal Malabsorption. R. H. Girdwood.—p. 53.
*Hyperpotassaemic Paralysis. G. M. Bull, A. B. Carter and K. G. Lowe.—p. 60.
Early Results of Resection for Pulmonary Tuberculosis. J. Dark and P. Jewsbury.—p. 64.
Amino-Aciduria in Lead Poisoning: Case in Childhood. V. K. Wilson, M. L. Thomson and C. E. Dent.—p. 66.
Pneumococcal Meningitis: Skull Defects as Aetiological Factor. W. H. Galloway and W. Chambers.—p. 68.
Primary Amyloidosis: Presenting with Peripheral Neuritis and Intractable Heart-Failure. S. J. Strich and G. Wade.—p. 70.

Folic Acid Excretion Test in Intestinal Malabsorption.—Girdwood points out that the term "sprue syndrome" has been used recently to include the features found in idiopathic steatorrhea of nontropical origin and in celiac disease. Since the introduction of the fat balance test of Cooke in 1946 it has been extended to include cases with megaloblastic anemia and deficient absorption of fat, but little other clinical evidence of intestinal malabsorption, and the term "malabsorption syndrome" has come into use. The seeming paradox of treating a condition believed to be due to malabsorption of hemo-

poietic factors by giving these same substances orally has led to the hypothesis that the fault in nontropical sprue is malabsorption of naturally occurring folic acid conjugates rather than of folic acid itself. The present investigation indicates that there is, in fact, considerable deficiency of absorption of folic acid in sprue, and that advantage can be taken of this to devise a test of folic acid absorption and excretion for the diagnosis of malabsorption by the small intestine. The author describes a comparison of urinary excretion of folic acid following subcutaneous and oral test doses of 5 mg. of folic acid in 11 cases of intestinal malabsorption, 15 cases of pernicious anemia, 14 controls, and 5 patients with pregnancy anemia. This test revealed impairment of absorption of folic acid only in patients with the malabsorption syndrome or with iron-deficiency anemia refractory to therapy with iron by mouth. Megaloblastic anemia of pregnancy subsequently responding to folic acid therapy may occur without biochemical evidence of a failure in absorption or tissue depletion of folic acid. Since it may be necessary in intestinal malabsorption to load the tissues with injected folic acid before performing the differential folic acid excretion test, time may be saved by doing this in all instances before the test is carried out. From the laboratory point of view a fat balance test is easier to perform, but it requires hospitalization of the patient so that a suitable diet can be given and its consumption supervised, and furthermore the stools must be collected for several days. The differential folic acid excretion test may be of particular value where steatorrhea is not obvious and there is refractory megaloblastic anemia, refractory iron-deficiency anemia, or unexplained glossitis. If further work confirms the value of the folic acid excretion tests, the diagnosis of sprue should, at least in some instances, be rendered easier in that special diet is not required and specimens of urine can be sent for assay from other hospitals to laboratories in which folic acid tests are being done. It is not yet possible to say whether a positive fat-balance test may be associated with a negative folic acid excretion test in the "malabsorption syndrome."

Hyperpotassemic Paralysis.—According to Bull and associates, much has been written in recent years about the dangers of a high concentration of potassium in the plasma, especially in the anurias, in Addison's disease, and following the administration of potassium. The greatest danger of hyperpotassemia is, of course, that of sudden death from cessation of heart action in diastole. Other features of hyperpotassemia are lassitude and clouding of consciousness, although these do not always occur. Finally, flaccid paralysis occurs rarely. The authors cite three patients with hyperpotassemic paralysis. In the first of these patients the paralysis recurred several times in the terminal stages of a subacute glomerulonephritis. In the second patient this symptom was present during an Addisonian crisis, from which he was rescued by appropriate therapy. The third patient, with renal failure due to renal tuberculosis, presented the symptom in the last days of illness. The mechanism of hyperpotassemic paralysis remains obscure, but it is suggested that it is an acute peripheral neuropathy.

Medical Journal of Australia, Sydney

1:721-756 (May 23) 1953

Accidents in Anaesthesia. C. N. Paton.—p. 721.
*Treatment of Carcinoma of Prostate with New Oestrogen, "TACE." H. Mortensen.—p. 728.
Common Eye Diseases in General Practice. A. Lamb.—p. 731.
Cystic Disease of Lungs. C. G. Bayliss.—p. 732.
Use of Pharmacological Relaxants in Psychiatry. S. P. Derham.—p. 736.

1:757-796 (May 30) 1953. **Partial Index**

Old Age: Clinical, Social and Nutritional Survey of Seventy Patients Over 65 Years of Age Seen in Hospital Out-Patient Department in Melbourne. E. G. Saint, H. F. Abrecht and C. N. Turner.—p. 757.
Exchange Transfusion and Transfusion in Infants and Young Children. J. C. A. Dique.—p. 764.
Observations on Leptospirosis in Victoria. W. J. Stevenson, L. Hayes, A. A. Ferris and N. A. M. Wellington.—p. 770.
Hydatid Disease at Royal Hobart Hospital. K. J. Friend and E. A. Lennon.—p. 772.

New Estrogen in Treatment of Carcinoma of Prostate.—When estrogen is used in the treatment of prostatic cancer, not only do the pressing clinical symptoms disappear and the metastases retrogress but microscopic examination of sections of the prostate after treatment may reveal no evidence of carcinomatous cells but rather a washed-out structure of large enucleated cells. It is now regarded that at least a contributory factor, if not the real cause of the relapse, in prostatic carcinoma being treated by estrogens, is hyperactivity of the hormonal phase of adrenal function. It has been proved experimentally that the continuous administration of the usual estrogens to laboratory animals causes enlargement of the pituitary and the adrenal glands. In the search for estrogens that did not have this stimulating effect on the adrenal and pituitary, studies were made with the estrogen chlorotrianisene (TACE). Although this drug produces characteristic estrogenic effects, it differs from diethylstilbestrol and hexestrol in that it does not have the same pronounced effect on the pituitary and the adrenals. The author cites animal experiments with this drug and describes his own clinical experiences with it. He has used the drug for only a short time and in a small number of cases. At first it was given in cases in which no further improvement could be achieved with estrogens commonly used. In other cases, the change to the new estrogen was made because of the painful and embarrassing manifestations of gynecomastia. The large, painful breasts and tender nipples in persons who take diethylstilbestrol over a long period of time often compel the reduction of the dosage, or the patient himself will cease taking the drug. The use of the new estrogen has invariably resulted in an amelioration of these distressing symptoms, and when used immediately after diagnosis, no evidence of feminization has been found or it has been very slight. The property of fat storage exhibited by the new estrogen seems to explain why it has a more prolonged effect. Because the drug is liberated slowly, the patient with prostatic cancer may develop a more constant level of estrogenic stimulation, which is more effective than the varying amounts of stimulation that follow the treatment with the estrogens in common use up to now.

Minerva Medica, Turin

44:1389-1436 (May 26) 1953. **Partial Index**

*Value and Limitation of Needle Biopsy in Diagnosis, Prognosis and Therapy of Hepatopathy: Personal Studies and Synthetic Review. M. Fazio and G. C. Angela.—p. 1389.
New (Preoperative) Laparoscopic Cholangiography by Means of Transparietal-Hepatic Puncture of Gallbladder: Preliminary Report with Description of Two Cases. M. Blanche and F. Muratori.—p. 1409.
Analysis of Alterations of Electrophoretic Serum Tracings in Patients with Hepatopathy: Suggestions for Their Physiopathological and Clinical Evaluation. E. Poli, R. Caspani, S. Jucker and A. M. Villa.—p. 1414.

Needle Biopsy of Liver.—The authors performed 108 needle biopsies of the liver with the technique of Iversen and Roholm in 77 patients. The biopsy diagnosis was confirmed by autopsy in all but one of the patients who died. This patient was a heavy drinker in whom diagnosis of pernicious anemia with indications of fatty cirrhosis of liver had been made. Autopsy revealed instead alcoholic steatosis with an occasional mesenchymal reaction of the portal-biliary spaces. The results of liver function tests coincided with the histological picture of the biopsy specimens in many patients, especially in those with nonfatty cirrhosis and neoplasms. Biopsy was the decisive diagnostic factor in patients with fatty cirrhosis and pure steatosis. Needle biopsy of the liver is indicated in all liver diseases of undetermined cause, in differential diagnosis between parenchymal and extrahepatic obstructive jaundice, and in primary or metastatic neoplasm of the liver. It is valuable in determining the type of cirrhosis present and in evaluating the course of chronic hepatitis and the effects of therapy in liver disease. Histological examination of serial biopsy specimens may reveal improvement in some instances in which laboratory tests do not reveal an improvement. Needle biopsy of the liver may also help in the diagnosis of some systemic disease. In fact, the changes that occur in the liver during infectious mononucleosis, diabetes, pellagra, and amyloidosis have already been studied by other authors. It is contraindicated in patients with a low prothrombin level. The authors never performed it in patients whose prothrombin concentration, as determined by Quick's method, was not above 40% of the normal. It is also contraindicated in patients with septic

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cholangitis, hepatic echinococcosis, bacterial or amebic abscesses, and ascites. Uncooperative patients and children are also, as a rule, excluded. The severest complication of needle biopsy of the liver is fatal hemorrhage. This is rare, and occurs mainly in patients in whom the prothrombin concentration was not considered. The authors had no complications in their patients.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

97:1241-1304 (May 16) 1953. **Partial Index**

Recent Developments in Eclampsia Problem. J. L. Mastboom.—p. 1250
*Habitual Abortion Resulting from Wide Uterine Isthmus (Internal Uterine Os). L. I. Swaab.—p. 1257.
Action of Isioniazid. H. L. Wolff.—p. 1262.

Habitual Abortion Caused by Wide Uterine Isthmus.—Swaab presents the case of a woman, aged 37, whose three previous pregnancies had resulted either in abortion or premature labor, despite treatment with vitamin E, progesterone and stilbestrol. Examination disclosed an abnormally wide internal uterine os and a lengthening of the isthmus, which had resulted from a previous curettage. In such cases the external uterine os is not necessarily ruptured and the uterine cervix when examined through a speculum may appear to be intact. The author shows the roentgenologic shadow of such a uterus side by side with that of a normal one, and he also shows a diagram of a cross section of such a uterus. The condition can be recognized when a uterine dressing forceps passes the internal uterine os (isthmus uteri) without difficulty. Rupture of the membranes prior to the onset of labor is characteristic of this condition. In the reported case the condition was corrected by surgical treatment, in which the cervix, particularly at the level of the isthmus, was narrowed with the aid of catgut sutures. Favorable results obtained by others with this intervention indicate a favorable prognosis.

Nordisk Medicin, Stockholm

49:769-802 (June 5) 1953. **Partial Index**

Use of Fruit Powder in Pediatrics in Treatment of Diarrhea. H. Keiser-Nielsen.—p. 803.
*Fetal Asphyxia and Its Treatment. F. Holtz.—p. 805.
Toxoplasmosis. E. Jacobsson.—p. 815.
*Long-Acting ACTH in Bronchial Asthma in Children. C. G. Bergstrand, I. Engström and S. Kraepelien.—p. 817.
Congenital Leukemia. F. Karlström.—p. 819.

Fetal Asphyxia and Its Treatment.—Fetal asphyxia occurred in 833 (2.25%) of 37,000 deliveries in the gynecologic department of the Södersjukhus from 1943 to 1951; 545 of the mothers were primiparas. In almost half the cases the fetal asphyxia was caused by prolonged labor; in one-third of the cases it was due to abnormally intensive uterine contractions. The commonest symptoms were changes in the rhythm and frequency of the fetal sounds and discharge of meconium. Ninety-eight cases (11.8%) were fatal. Treatment consists in the first place in prophylactic measures to promote delivery before fetal asphyxia occurs. Intense pains threatening to cause fetal asphyxia can be subdued by narcosis and confluent pains be limited by injections of morphine. Fetal mortality is decreased by more active management of labor. Interventions necessary to save the life of the fetus play an important part in the prognosis. If an intervention is not possible, heart activity may be stimulated by injections of heart stimulants to the mother. Asphyxia after birth is treated according to the nature of the case. In 553 cases removal of mucus from the respiratory passages gave good results. Cyanosis in 144 cases in which the infant was blue was treated by various measures, including agents stimulating heart and respiratory activity, with favorable results, and in 38 of the 79 cases in which the baby was white treatment with artificial respiration, heat, and oxygen was successful.

Long-Acting Corticotropin in Bronchial Asthma in Children.—Bergstrand and his associates administered corticotropin (ACTH) with prolonged action to 11 children, aged from 5 to 13, with grave asthma of long standing resistant to the usual antiallergic treatment. Thirteen asthmatic children, aged from 4 to 14, were treated with the regular corticotropin preparation. If a rapid corticotropin effect is desired in asthmatic attacks endangering life, regular corticotropin is preferred. To break a long-continued status asthmaticus, treatment with either the regular or the long-acting corticotropin can be applied with about the same favorable temporary effect, improvement as a rule setting in more slowly with long-acting corticotropin. With this preparation, however, ambulant treatment is possible, which means a limited number of injections, at intervals of days, and a comparatively small dose, reckoned by the day, and allows treatment for longer periods without too great danger of side-effects.

Policlinico (Pract. Sect.), Rome

60:841-872 (June 15) 1953

Toxic Action of Chlortetracycline (Aureomycin) in Guinea Pigs. F. Giunchi, A. Fidanza, L. A. Scuro and others.—p. 841.
*Gamma Globulin, a Blood Derivative, in Therapy. V. Lamarca.—p. 847.
Subcutaneous Calcification with Rare Course: One Case. L. Cancellotti.—p. 853.

Gamma Globulin in Therapy.—One of the latest discoveries in the field of immunology is the identification of antibodies with gamma globulin of human serum. This achievement explains the increased emphasis on and interest in this important blood derivative. Gamma globulin was first used as a prophylactic against measles in 1938. It prevented the onset of the disease if it was inoculated within five days from the date of exposure and gave only partial immunity if it was given later. It proved especially valuable in children in poor general condition with tuberculosis and acute respiratory disease who had been exposed to the infection. Passive immunization lasted for two to three weeks, with the patient's age, degree and duration of exposure, virulence of the virus, and individual condition of immunization playing a great part on the outcome of the therapy. Since gamma globulin contains not only specific antibodies against measles but also a wide range of other antibodies, it was later used for passive immunization against other infections. It gave good results in whooping cough, epidemic parotitis (by preventing onset of orchitis), epidemic or infectious hepatitis, and post-transfusion hepatitis. It was used later in sepsis of infants and roseola infantum. The greatest usefulness of gamma globulin, however, is as a prophylactic against poliomyelitis. This is based on the concept that most human beings overcome the infection without the paralytic symptoms that are characteristic of the disease. This occurs because the virus enters the organism but does not reach the nervous tissue. The infection thus does not become manifest, but specific antibodies are formed. Preliminary reports from the United States, where research studies and experiments are being carried out on a large scale, indicate that passive immunization against poliomyelitis was secured with gamma globulin for at least five weeks. These results are encouraging, but a longer period of observation and further studies are needed for a final evaluation.

Presse Médicale, Paris

61:863-880 (June 17) 1953

Experimental and Clinical Study of a New Chemotherapeutic Agent in Tuberculosis (Glycuronolactone Isonicotyl-Hydrazone). G. Brouet, B.-N. Halpern, J. Marche and J. Mallet.—p. 863.
Value of Skin Thermometry in Investigation of Various Conditions, Especially Vascular Disturbances in the Limbs. G. Tardieu and M. Garoit.—p. 866.
Simultaneous Study of Skin and Muscle Temperatures in Normal Subjects. J. Oudot, J. Natali and C. Marceau.—p. 868.
The Focal Lesion: Pathological Manifestation of a Neurovegetative Injury. A. Bernard.—p. 872.
New Conceptions of Physiopathology and Treatment of Tissue Lesions of Vasomotor Origin, Especially in Relation to Arteritis. H. Reboul, P. Laubry and L. Vergoz.—p. 875.
*Prolonged Sleep Treatment in Medicopsychiatric Practice by So-Called Hibernation Method. A. Deschamps and M. Cadoret.—p. 878.

Prolonged Sleep (Hibernation Method) in Psychiatric Medical Treatment.—Prolonged sleep as used by the authors differs from artificial hibernation because it is induced principally by drugs, and refrigeration is used merely as a supplementary measure. The depth of the sleep and the duration of the treatment are less important than the degree of relaxation secured.

Treatment by this method proved safe even in aged, hypertensive, and cardiac patients. Strict medical supervision is required, and the ganglion-blocking agents used to obtain neurovegetative inhibition should be withdrawn gradually at the close of the treatment. The sleep produced is calm, and the patients are relaxed and indifferent. Breathing is regular, the pulse is usually normal, and there is almost always a drop in the blood pressure. Prolonged sleep was used in treating 15 patients with various psychiatric conditions who had not been benefited by other methods of treatment or whose general condition was too poor for shock therapy. The best results were secured in patients who had symptoms of agitation and confusion and severe melancholic anxiety, but substantial improvement was also noted in patients with mania.

61:881-900 (June 20) 1953

*Statistical Study of Late Results of Surgical Treatment of Epilepsy. J. Guillaume, G. Mazars and Y. Mazars.—p. 881.
"Filled Up" Tuberculous Cavities of the Lungs. A. Bernou, J. Tricoire and J. Tournier.—p. 883.
Nocturnal Acroparesthesias and Their Treatment by High Frequency Currents. R. Lacassie.—p. 884.

Late Results of Surgical Treatment of Epilepsy.—Of 110 patients between the ages of 4 and 49 years who had focal cortical epilepsy demonstrated by an abnormal electrical activity originating from a limited point or zone of the cerebral cortex and who had been operated on and followed up postoperatively for from six months to four years, 82 had obtained good or excellent results. Of the 82 patients, 27 no longer had convulsions despite complete discontinuation of drugs, and they did not have any sequelae; 27 patients had no sequelae and no longer had convulsions but still required administration of a reduced dose, 0.10 gm., of phenobarbital sodium; 9 patients no longer had convulsions but persistent neurological sequelae that were compatible with a good social readaptation; the remaining 19 patients had one or two attacks of convulsions in the course of one year. Twenty-three patients were improved having less attacks of convulsions despite the administration of a reduced dose of drugs as compared to the time before the surgical intervention. Five patients were therapeutic failures; one died, one became worse, and three were unchanged. The author emphasizes that the patient operated on had had persistent attacks of convulsions despite prolonged treatment with antiepileptic drugs. The selection of patients for surgical intervention was based essentially on electroencephalographic criteria. Surgical intervention was carried out under corticographic control following excision step by step until any abnormal electrical activity had disappeared. Partial or complete therapeutic failures were essentially due to the impossibility of proceeding with the resection of the epileptogenous cortical area without running the risk of producing some motor weakness, sensorial diminution, or a disturbance of speech when a significant zone of cortical representation had been invaded by the eliptogenous area. Considering the benign character of the surgical intervention and the favorable results obtained in patients with severe cortical epilepsy, it seems justified to extend surgical treatment to less serious cases provided that the electroencephalographic criteria prove particularly favorable. By extending the indications for surgical intervention it may be possible to detect and to apply treatment to a tumor with a slow course whose only clinical manifestation consists of a convulsive state.

Riforma Medica, Naples

67:597-624 (May 30) 1953

Surgical Treatment of Tumors of Bladder. M. Sorrentino.—p. 597.
Procaine Amide in Therapy of Supraventricular Paroxysmal Tachycardia. A. Tommaselli.—p. 601.
*Insufficient Use of Active Therapy in Chronic Pulmonary Tuberculosis. G. Censi and P. Maraschio.—p. 607.

Inadequate Treatment of Chronic Pulmonary Tuberculosis.—Although the mortality rate for pulmonary tuberculosis in Italy has decreased, the average period of treatment and hospitalization for patients with the disease has increased. Therapy with antibiotics did bring about rapid and frequent recoveries, but sooner or later there were relapses with more and larger cavities that prolonged the course of the disease. Incompetence of the phthisiologist in selecting the best treatment, inadequate psychological preparation of the patient, inadequate surgical equipment, and economic factors are responsible for this discouraging situation. Chronic cavities can be eliminated definitively with proper and timely surgery. Divergencies that arise on the selection of the best surgical procedure are easily eliminated if treatment is individualized and the method that guarantees the best results with the least risk is applied. Pulmonary resection and collapse therapy are the treatment of choice in chronic pulmonary tuberculosis. The former is especially indicated in patients whose lung tissue is destroyed, those with stenosis of the main or the lobar bronchus, and those with tuberculoma. The collapse therapy should be employed in patients in whom the resection is contraindicated. It gives better results than intrapleural or extrapleural pneumothorax. A review of the literature revealed that, of 100 patients in whom pulmonary resection was performed after streptomycin became available, only 7 had died within three years, whereas, of 100 patients who were treated medically in sanatoriums before the antibiotic era, only 24 were still living five years later. Of 100 patients in whom pneumothorax was induced before streptomycin became available, 45 died within five years, whereas, of 100 in whom lobectomy or pneumonectomy was performed, only 13 had died two to four years later. Approximately 90% of the patients with chronic pulmonary tuberculosis can be cured with pulmonary resection, if it is performed before any other surgical treatment and before resistance to antibiotic therapy has developed.

Schweizerische medizinische Wochenschrift, Basel

83:551-570 (June 13) 1953

Chemotherapy of Tuberculosis. H. Staub.—p. 551.
*Endangiitis Obliterans of Kidney and Hypertension. H. Fellmann and H. U. Zollinger.—p. 556.
Type and Form of BCG Skin Lesion. F. Puntigam and K. Berger.—p. 559.
*Hormonal Regulation of Dentition. L. J. Baume.—p. 560.

Endangiitis Obliterans of Kidney and Hypertension.—Fellmann and Zollinger report two patients with endangiitis obliterans and involvement of the kidneys. In one of these the blood pressure remained normal while the necropsy revealed very extensive, but rather recent renal infarcts. The second patient died with signs of malignant hypertension. In this patient, autopsy disclosed multiple fresh renal infarcts interspersed with ischemic areas of the parenchyma. The latter were apparently result of subtotal arterial obliteration by endangiitic lesions. The authors point out that for decades after endangiitis obliterans had been described by von Winiwarter and Buerger, it was considered chiefly a disease of the arteries of the extremities. During the last two decades more and more observers have called attention to the involvement of vessels of parenchymatous organs. The existence of "coronary" Buerger's disease has been established beyond a doubt, and cerebral involvement has likewise been established. Reports about endangiitis obliterans of the kidney have been so far rare.

Hormonal Regulation of Dentition.—Baume chose the incisors of rats to study the hormonal regulation of dentition. These have the advantage that the eruption is continuous and is not limited to a certain period as is the case in human beings. The following three experiments were made: 1. Thyroidectomy was done on the day of birth, and subsequently the animals were treated with growth hormone and thyroxin. 2. Hypophysectomy was done on the 28th day and the animals were observed for various periods of time. 3. Growth hormone and thyroxin were administered following hypophysectomy. It was found that hypophysectomy had a more decided effect on dentition than did thyroidectomy. The hypophysis influences dentition not only by its thyrotropic, but also by its growth hormone. Thyroid hormone and hypophyseal growth hormone have fundamentally differing effects on dentition. Thyroid hormone influences the size as well as the eruption of the tooth and is the most important hormonal factor in dentition. It has a specific effect on histological differentiation of the epithelium and is capable of inducing the formation of bone tissue in the growth cartilages; for this reason it has been

designated as the maturation hormone. Its general stimulating effect on the metabolism produces increased vascularization in the dental tissue. While the growth hormone has a much more decisive effect on the size of the tooth than does thyroxin, it is not able to promote tooth eruption following hypophysectomy. As an activator of the protein metabolism thyroxin has a stimulating effect on all mesenchymal tissues and has a special affinity for the cartilaginous growth disks. In the described experiments this became manifest in the activation of pulpa growth, in dentinogenesis and in the membranous bone growth of the alveolar process. The mechanism of tooth eruption cannot be completely dissociated from growth, in that proliferation of the odontogenic tissue is the basic process, and in this the growth hormone is most important. To insure that the tooth not only increases in size but also erupts, the dental and peridental tissues require a different tempo of growth. The organ which determines this differentiation is definitely the odontogenic epithelium, which is regulated by the thyroid hormone. Deficiency of this hormone causes disturbances in the proliferation of the odontogenic epithelium, and this in turn causes primary malposition of the tooth papillae and later inhibition of eruption. Retarded eruption of the tooth germ with continued root growth suggests mild hypothyroidism, provided that rickets, vitamin A deficiency and sternocleidocranial dysostosis can be ruled out. Treatment with thyroid extract will stimulate the eruption of these retained teeth, provided treatment is tolerated long enough. Generally retarded eruption with greatly retarded germ development is suggestive of cretinism, and requires on the basis of experimental observation combined administration of thyroid extract and growth hormone.

Semaine des Hôpitaux de Paris

29:1953-1986 (June 14) 1953

*Efficacy of Massive Doses of Vitamin B_{12}. P. Chevallier.—p. 1953.
Treatment of Poisoning by Phosphoric Ester Insecticides. R. Fabre.—p. 1957.
Potassium Metabolism and Its Changes Following High Doses of Desoxycorticosterone. H. Naegeli, R. S. Mach and E. Mach.—p. 1959.
Electrical Data in Mitral Heart Disease: Clinical, Anatomical, and Operative Comparisons (115 Cases). E. Donzelot, R. Heim de Balsac, G. Dauzier and others.—p. 1968.

Efficacy of Massive Doses of Vitamin B_{12}.—Small doses of vitamin B_{12} may benefit convalescent patients and others whose need for the vitamin is not absolute, but when it is imperatively required, it should be given in massive doses. A single intramuscular injection of 1,000 mcg. of crystalline vitamin B_{12} has been found adequate to maintain a normal blood and marrow picture for from 128 to 358 days in 15 patients with pernicious anemia, indicating that the vitamin can be stored in the body. Similarly large doses have also proved effective in various neurological and rheumatological conditions, such as multiple sclerosis, polyneuritis, and trigeminal neuralgia. Vitamin B_{12} is well tolerated and, like other members of the vitamin B complex, entirely nontoxic, whether given orally or parenterally. Marked improvement and in some cases an apparent cure of progressive pernicious anemia has been secured by the daily administration of 1,000 mcg. When given intramuscularly, injections of 1,000 mcg. every other day are enough to produce satisfactory results in ordinary cases without severe nervous complications. The use of vitamin B_{12} in massive doses is economically advantageous because it shortens the period of hospitalization and frequently results in cure of the patient.

29:2061-2126 (June 22) 1953. **Partial Index**

Examination of Patient with Mitral Stenosis with a View to Operation. P. Soulié, R. Tricot and J. Di Mattéo.—p. 2063.
Preoperative and Postoperative Hemodynamic Study of Mitral Stenosis. J. Carlotti, J. Joly, J. R. Sicot and G. Voci.—p. 2079.
*Immediate Postoperative Results of Commissurotomy. Y. Bouvrain, P. Fortin and J.-L. De Vahia.—p. 2097.
*Late Results of Commissurotomy and Its Indications. P. Soulié, F. Joly, J. Carlotti and J. Baillet.—p. 2105.

Immediate Postoperative Results of Commissurotomy.—The immediate postoperative results of commissurotomy fall into three groups: (1) the inevitable disturbances and discomforts of the first few days after the operation; (2) complications of varying severity; and (3) deaths. The postoperative course in favorable cases is comparatively uneventful. Fever, which is constantly noted, is of short duration; the pain caused by the operative wound usually diminishes rapidly; pleural effusions require from two to five tappings; and the pericardial reaction is latent and can only be detected in roentgenograms. Patients may be allowed up in about a fortnight and can leave the hospital three or four weeks after the operation. Many continue to have parietal pain in the scapular region for some time and find it difficult to move the left shoulder. Disturbances of cardiac rhythm, thromboembolic accidents, and acute postoperative pulmonary edema are the principal complications observed during the first four to six weeks after surgery. The first two can often be corrected by appropriate treatment, but the third indicates that the operation aggravated an existing mitral regurgitation. No matter how great the skill and the experience of the surgeon, there are cases in which the valves are so profoundly altered and ineffective that intervention will inevitably increase the systolic reflux. Postoperative deaths may be due to embolism, cerebral thrombosis, or the existence of irremediable changes in the mitral valve. A syndrome of cyanosis during surgery and postoperative collapse causing death within 48 hours has also been observed. This syndrome apparently occurs when mitral stenosis is accompanied by high pulmonary hypertension with an elevated arteriocapillary pressure gradient and extensive pulmonary lesions. Autopsy showed the lungs of patients in whom this was observed to be hypervascularized, brownish, firm, and resistant. All efforts at therapy were ineffectual, and the appearance of cyanosis at the beginning of anesthesia should be taken as an indication for abandonment of the operation.

Late Results of Commissurotomy and Its Indications.—Four classes of patients with mitral stenosis may be subjected to commissurotomy. Class 1 includes patients with little functional disturbance in whom cardiac catheterization shows elevated pressures and in whom electrocardiography indicates that the right side of the heart is being subjected to strain. Commissurotomy in these patients is a preventive measure and the mortality accompanying it should be negligible. Patients in class 2 have severe dyspnea or suffer repeated attacks of pulmonary edema. The hemodynamic disturbances revealed by catheterization of these patients are severe, and their functional incapacity is complete. Commissurotomy gives excellent results in three-fourths of these cases, and the operative mortality does not exceed 4%. The operative indications in class 3 patients are the most difficult to determine. Functional disturbance is severe, and mitral stenosis has usually resulted in the first stages of cardiac insufficiency. The operative risk in these patients is great and results in a mortality rate of from 15 to 20%; excellent results, however, are sometimes obtained. Class 4 patients are those with total arrhythmia, severe heart failure of several months' or years' duration, and greatly enlarged hearts; their condition is sometimes improved by the operation, but the operative mortality is very high. Commissurotomy should not be a routine procedure in mitral stenosis; the benefit to be expected from it and the risks accompanying it should be carefully evaluated with due regard for the fact that in spite of their disability many patients with mitral stenosis reach the age of about 60 with medical treatment alone.

Tidsskrift for Den Norske Laegeforening, Oslo

73:437-476 (June 1) 1953. **Partial Index**

*Prognostic Significance of Small Tumor in Cancer of Breast. L. Kreyberg and T. Christiansen.—p. 437.
Medical Control of Hospital Personnel Exposed to Radiation. P. Sundby.—p. 440.
Cancer of Cervix as Complication in Delivery. K. W. Skarsten.—p. 448.
Cystic Pyeloureterocystitis. A. Sanderud.—p. 449.

Prognostic Significance of Small Tumor in Cancer of Breast.—In Kreyberg and Christiansen's 974 cases of cancer of the breast examined from 1933 to 1942, which allowed at least 10 years' observation of the later fate of the patients, there were only 56 carcinomas (5.7% of the entire number) of the size of a hazel nut or smaller, and only 10 were as small as a pea

or a bean. The authors conclude that over half of the patients with cancer of the breast having a tumor of the size of a hazel nut or smaller will succumb to the disease after receiving the treatment applied today. This is true even for the smallest tumors in the series; of the 10 patients with such tumors 5 are living after 10 years and 4 have died from metastases. The minimal cancers of the breast do not as a group definitely give a better prognosis than does an ordinary average group of cancers of stage 1 and stage 2 that receive the same treatment.

Tubercle, London

34:151-178 (June) 1953

Use of Benemid to Enhance Blood-Levels of Sodium Para-Aminosalicylate (PAS). J. A. McLeod, F. W. A. Turnbull and J. W. Crofton. —p. 152.
Correlation of Quantitative Mantoux Reactions with Clinical Progress in Pulmonary Tuberculosis. H. M. Turner.—p. 155.
Two Cases of Neutropenia in Children Possibly Due to Streptomycin and P.A.S.A. Therapy. R. Wilder.—p. 163.

Ugeskrift for Laeger, Copenhagen

115:879-918 (June 4) 1953. **Partial Index**

*Poliomyelitis Epidemic in Copenhagen in 1950. R. Bjerglund and H. O. Bang.—p. 879.
*Cardiac Affection in Poliomyelitis. J. Georg, T. Hilden and B. Vimtrup. —p. 886.
Progressive Exophthalmus: Muscular Changes and Thyrotropin Content in Serum. G. Asbol-Hansen, K. Iversen and R. Wichmann.—p. 889.
Cause of Appendicitis. S. Müller.—p. 895.
Allergic Children: Work in Rigshospital's Polyclinic with Children with Allergic Diseases and Value of Cooperation with Physicians Sending Children. K. Wilken-Jensen.—p. 897.
Cancer in Middle Ear. H. K. Kristensen.—p. 899.
Application of Serum and Vaccine Against Tetanus. H. Andersen. —p. 906.

Poliomyelitis Epidemic in Copenhagen in 1950.—From late June, 1950, to the end of the year 110 cases of paralytic and 636 cases of nonparalytic poliomyelitis were treated in Blegdam Hospital. Children predominated, and there was a slight preponderance of males in the nonparalytic cases. The frequency of paralysis, in 15% of the entire group, the degree of severity, and the mortality increased with increasing age. Pregnancy seemed to increase morbidity and frequency of paralysis. There were also 136 cases of probable poliomyelitis, and 19 cases of polyradiculitis are considered because of their occurrence during the epidemic period. The epidemic curve reached its peak in September. The epidemic curve for polyradiculitis corresponded to that for poliomyelitis, but the age average was higher than that in poliomyelitis.

Cardiac Affections in Poliomyelitis.—In the opinion of Georg and his associates a specific myocarditis may perhaps occur in some cases of poliomyelitis, but the majority of the histological and electrocardiographic changes described in this disease can undoubtedly be explained as results of anoxia and disturbances in the pulmonary circulation in patients with respiratory difficulty.

Wiener medizinische Wochenschrift, Vienna

103:449-490 (June 20) 1953. **Partial Index**

*Peripheral Endobronchial Plasmacytoma of the Lung with Hypertrophic Osteopathia. A. Plenk and K. Pretl.—p. 450.
Pendiomid-Ciba 9295, a Ganglion-Blocking Substance, in Urologic Diseases and Operations. H. F. J. Weber.—p. 451.
Plastic Surgery with Direct Pedunculated Cutaneous Flap. J. Böhler. —p. 453.
Spontaneous Pneumothorax. L. Neuner.—p. 455.
*Pheochromocytoma and Hypertension. H. Hartl.—p. 467.

Plasmacytoma of the Lung.—The occurrence of an extramedullary plasmacytoma of the lung, a relatively rare tumor, is reported in a 16-year-old girl. For about one year the patient had transitory painful swellings of the fingers, occasional pains in the arms and legs, occasional night sweats, and lancinating pains in the area of the right shoulder on respiration. A round shadow the size of an apple was demonstrated on roentgenologic examination in the area between the middle and lower lobe of the right lung. The blood count revealed normal number of erythrocytes and leukocytes; changes of the albuminoid bodies could not be demonstrated. Roentgenologic examination of the skeleton revealed stratified periosteal bony cuffs on the phalanges of the fingers and on the metacarpal bones of the hands, as well as on the ulna and on the radius. An endobronchial plasmacytoma of the lower lobe of the right lung was removed by lobectomy. The postoperative follow-up was much too short for the morphological disappearance of the new growth of bone, but the patient no longer complained of pain. The hyperplastic osteopathy is a valuable symptom in the diagnosis of pulmonary tumors. Microscopic differentiation between metastasizing and benign tumors is not possible. New foci may occur by metastasis despite the distinct demarcation of the plasmacytoma. Radical treatment by surgical removal of the tumor is advocated.

Pheochromocytoma and Hypertension.—According to Hartl, the incidence of pheochromocytoma is higher than it is generally assumed. Hypertension may be caused by a pheochromocytoma in about 0.5% of all patients with hypertension. Paroxysmal episodes of hypertension are not the only characteristic of pheochromocytoma, since in most patients the tumor may cause a persistent, labile hypertensive state. Pheochromocytoma should be thought of in the differential diagnosis of a patient with hypertension. Diagnosis of pheochromocytoma may be aided by the modern chemical tests with such substances as histamine, metacholine chloride, epinephrine, or tetracthylammonium chloride. These tests are not specific for pheochromocytoma and not free of risk. Tests with adrenolytics, such as Dibenamine (N,N-dibenzyl-β-chloroethylamine) hydrochloride may be of even greater aid in the diagnosis, but in the author's experience pneumoradiography of the retroperitoneal space after parasacral injection of air is the method of choice in demonstrating the tumor, because both adrenals may be visualized in one stage and the risk of air embolism is less than with the injection of air into the perinephric area. Surgical removal of the pheochromocytoma is not difficult, but the labile blood pressure makes the anesthesiologist's task difficult. Administration of Dibenamine preoperatively and in the course of the intervention may prevent a catastrophe due to liberation of epinephrine caused by manipulation of the tumor. Arterenol provides protection against reactive hypotension. Despite the microscopically benign findings, pheochromocytoma should be designated as "functionally malignant," since death may result within a short time if surgical removal is not carried out. Seven illustrative cases are described in five men between the ages of 20 and 42 and in two 30-year-old women. In one of these the tentative diagnosis of pheochromocytoma could not be confirmed on necropsy. Three patients, one of them with a mixed type of pheochromocytoma and adrenal cortex tumor, made a complete recovery after surgical removal of the tumor.

Ztschr. f. d. ges. innere Medizin, Leipzig

8:333-380 (April 15) 1953. **Partial Index**

Resorption, Transport and Storage of Iron. K. Konitzer.—p. 333.
*Physiology of Blood Transfusion: Stress Effect. H. Möller and W. Wendland.—p. 339.
Clinical Forms of Endarteritis Obliterans and Its Differential Diagnosis. R. Julitz.—p. 343.
Laparoscopy: Its Importance for the Internist. K.-H. Straube.—p. 361.
Problems of Virus Influenza with Especial Consideration of Disorders of the Central Nervous System. A. Sylla.—p. 369.

Stress Effect of Blood Transfusion.—Möller and Wendland discuss the fate of some of the constituents of transfused blood, particularly of the protein, and the effects of the transfusion on the bone marrow, blood picture and circulation. They believe that blood transfusion produces a stress reaction. Determining the eosinophil counts of 10 patients, they found that in 8 the transfusion was followed by a noticeable decrease in eosinophils. They investigated the excretion of 17-ketosteroids in the urine in seven patients and found a noticeable increase following transfusion in five of these. Either a decrease in eosinophils or an increase in the elimination of corticoids was observed in 15 of 17 patients after blood transfusion. Possibly some of the effects of blood transfusion represent reactions typical of Selye's adaptation syndrome; these include changes in the blood and plasma volumes,

disturbances in the permeability of the cell membranes and of the capillaries, increase in diuresis, changes in the blood pressure, in the proteins, in the blood picture and in the bone marrow. According to Selye, the picture of the adaptation syndrome rarely appears in the pure form, but it is partly obscured by the specific effect of whatever agent is active. This masking by the specific effect of blood transfusion makes evaluation difficult.

8:381-428 (May 1) 1953. **Partial Index**

Graham's Anastomosis in Gastrectomy. M. Steingräber.—p. 381.
Cytomorphologic Changes of Bone Marrow and Changes in Blood Protein Picture in Reticuloses. R. Emmrich and E. Perlick.—p. 401.
*Erythrocytopathia Punctata Granuliformis in an Adult. J. Brugsch and E. Tichter.—p. 411.
Is the Supreme Law of Physician "Nil nocere" Compatible with Use of Manzullo Test? Question of Tellurite Poisoning. C. B. F. W. Ahrens.—p. 418.
Influence of Antibiotics and Chemotherapeutics on Biliary Pigment Reactions. H. Göhr, T. Görges and F. J. Diensberg.—p. 421.
Primary Double Carcinomas. H. Wiesner.—p. 426.

Erythrocytopathia Punctata Granuliformis in an Adult.—Brugsch and Tichter describe a new entity to which they apply the term "erythrocytopathia punctata granuliformis." The disorder was observed in a woman, aged 42, but the authors feel that it is related to an anemia of the newborn, in which the erythrocytes are characterized by the presence of inclusion bodies, and which was described by Gasser and Willi. In the woman, whose history is presented, the erythrocytes of the peripheral blood disclosed spontaneous formation of Howell-Jolly bodies, appearance of normoblasts, target cells, macrocytes, and reduction in osmotic resistance. Although there was no aplasia of the spleen, as Gasser and Willi had observed in their cases, splenic dysfunction could be suspected in the presence of hepatic cirrhosis with severe changes in the blood proteins. Malformations of the blood vessels (multiple hemangiomas) and defective toes were present. These and other defects in a woman, who was born of consanguineous parents, suggest severe generalized cellular abnormalities, and it is suggested that a generalized disturbance existed in the synthesis of proteins or of ribonucleic acid. The granula of the lymphocytes also showed abnormalities. The authors feel that in their patient the hepatic disorder, hypothrombinemia, and changes in the blood proteins with gamma-hyperglobulinemia were of importance in the pathogenesis. Splenic disturbances in cases of this type presumably are not the essential cause, but only an important eliciting factor. The high nucleosidase content of the spleen might be related to the decomposition of erythroblastic nuclei in the bone marrow. Formation of defective erythroblasts with pathological protein and nucleoside formation would then promote the formation of Howell-Jolly-like bodies in the presence of dysfunction or even agenesia of the spleen.

8:477-524 (June 1) 1953. **Partial Index**

Contribution to Experimental Osteomyelitis and Its Treatment with Penicillin. G. Rothe and F. Flemming.—p. 477.
Clinical Significance of Methodology of Clearance for Functional Kidney Tests with Particular Consideration of Differentialdiagnostic Problems; Third Communication: Endocrine Diseases. H. Dutz.—p. 482.
*Clinical Observations of Side-Effects of Isonicotinic Acid Hydracid Preparations. G. Pickroth.—p. 494.
Behavior of Mineral Level in Blood Serum After Injection of Tetraethylammonium Bromide. H. Kleinsorge and K. Linde.—p. 499.

Side-Effects of Isoniazid Preparations.—Isoniazid was given first in doses of 10 to 15 mg. and later in doses of 5 to 6 mg. per kilogram of body weight, daily in four divided doses, to 147 adult patients with pulmonary tuberculosis of all types, including those with exudative pleurisy. Fatigue and somnolence were noted most frequently during the first days of treatment. In 6 patients these phenomena continued for three weeks. The incidence of these side-effects was higher with the dose of 10 mg. per kilogram of body weight than with the smaller doses. Fatigue and sleepiness in an 18-year-old girl were associated with refractory constipation and disturbances of micturition during the first five days of treatment. Sensations of burning, furred feeling, formication, smothering, and lancinating pains in hands and feet were observed in 16 patients. These paresthesias occurred after four weeks of treatment (14.5 gm. of the drug) at the earliest and after six months of treatment (73.9 gm.) at the latest. They occurred in 11 patients after three months of treatment. The paresthesias subsided very slowly. Administration of nicotinic acid amide, and a proprietary crystalline vitamin B_1 (Betabion) proved ineffective except in one patient. Twenty-one patients complained of dizziness, 5 of headache, and 11 of a sensation of pressure in the frontal region of the head. Seven patients had transient palpitation, and in one patient with arteriosclerosis complaints of an angina pectoris type required discontinuation of the drug. Eczema, rash, and pruritus occurred in six patients. Five patients complained of nausea and occasional vomiting during the first weeks of treatment; in one patient these side-effects recurred after three and a half months of treatment and required discontinuation of the drug. In only seven patients a serious condition developed consisting of mental confusion, meningism, circulatory disturbances, and polyneuritis. The author believes that there is a relationship between incidence and severity of the side-effects and the dosage of the drug and partly also of the type of the tuberculous disease. The side-effects probably depend on the length of time the drug is administered. Arteriosclerotic changes and previous damage due to drugs or disease may favor the occurrence of untoward reactions. A specific therapy does not seem to be effective. In two of the author's patients manifestations of polyneuritis did not subside for many months after discontinuation of the drug. The side-effects of isoniazid are not entirely harmless. Despite that, treatment in a hospital or sanatorium may be continued in ambulant patients provided that the patient's condition will allow it and definite control of the patient is guaranteed.

Ztschr. Tropenmed. u. Parasitol, Stuttgart

4:285-414 (June) 1953. **Partial Index**

Problems of Immunity in Malaria. E. G. Nauck.—p. 285.
*Arthropods as Hosts of Causal Agent of Q Fever (Rickettsia burneti). F. Weyer.—p. 344.
*Rabies: Morbidity and Mortality in Exposed Persons. L. Gremliza.—p. 382.

Causal Agent of Q Fever (Rickettsia burneti): Arthropods as Hosts.—Weyer describes experiments on bloodsucking arthropods to ascertain whether or not they were potential hosts of Rickettsia burneti and thus may become vectors of Q-fever. Ticks (Ornithodorus moubata), body lice, fleas, bedbugs, and larvae of meal worms were infected with rickettsial material by sucking or by intrarectal and intraperitoneal application. Whereas, under natural conditions, Rickettsia burneti is found only in various species of ticks, all of the above named arthropods proved more or less susceptible when experimentally infected. Rickettsias multiplied rapidly in the coeloma and intestinal cells without serious damage to the host; they also spread occasionally to other organs and were excreted with their virulence unchanged. Contrary to other rickettsias, Rickettsia burneti seems highly adaptable to various organs and cell types of heterogeneous arthropods, most of which, however, do not act as natural hosts, carriers, or transmitters. Considering the favorable conditions for the survival of Rickettsia burneti, one wonders why Q-fever is not more prevalent.

Rabies: Morbidity and Mortality in Exposed Persons.—Of 32 persons attacked by a rabid wolf in a rural district in Persia, 19 were bitten about the head, 3 on face and neck, and 10 on hand or arm. Four of the six who received antirabic treatment remained free from symptoms and two died. In the two treated patients who died symptoms of the disease were evident before treatment was begun. Of the 26 patients who received no antirabic treatment, 13 died and the other 13 remained free from symptoms and survived. The mortality rate was over 50% among the patients who had been bitten on face, scalp, or neck; in those who received bites on arm or hand the mortality was lower. The incubation period averaged 24 and 27 days after head and neck bites, respectively, and 45 days after arm and hand bites. It is pointed out that even severe lacerations caused by rabid animals do not necessarily lead to death when left untreated. Similar conclusions were reached by another investigator who reported on human rabies resulting from the bites of rabid wolves in February, 1952.

BOOK REVIEWS

Practice of Psychiatry. By William S. Sadler, M.D., F.A.P.A., Consulting Psychiatrist to Columbus Hospital and Pinel Sanitarium, Chicago. Cloth. $15. Pp. 1183. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1953.

Dr. Sadler is one of the grand old men of American psychiatry, having begun his contributions to the literature more than 40 years ago. He has done much to popularize psychiatry, not only among the laity but among nonpsychiatric practitioners as well. In this contribution, he has attempted to give us a "book to serve as a ready and compact reference for diagnosis and immediate treatment." What he has given us actually is a great collection of data from his active professional life of many years. The result is an almost overwhelming collection of facts, theories, and personal opinions combined in an interesting style that belongs to another age of medical writing. One can hear Sir William Osler in the following quotation: "After two or three visits with the patient, I concluded there must be something on her mind, and, discerning to disposition on her part to disclose it, made bold to probe more deeply; finally, when she was asked whether she was worrying over autoeroticism or over some slip of propriety in her relations with her lover, she indignantly denied the latter and tacitly admitted to the former."

The final result is unique. The book is not a reference book, a textbook, or a manual, despite its attempts to be all these things; it is a compendium of psychological and psychiatric knowledge since the time of Adam. In this sense it is a historical survey of interest to psychiatrists and workers in this field but certainly neither a textbook for students of medicine nor a manual for practitioners. Dr. Sadler's book includes such interesting chapter headings as: "Psychiatry and Psychiatrists," "Mental and Emotional Mechanisms," "The Health and Happiness Pathoses," "What Is Personality?" "The Sexual System," "Therapeutic Study Program," "Philosophy and Religion," and "Will-Power and Decision." There are 75 chapters, a 40 page appendix, "Schools of Psychiatry," and an extensive glossary.

That such a work, covering almost 1,200 closely printed pages, must contain much that is questionable and must often consist of a synthesis of the thoughts of others is inevitable, because no one can have accurate and sensible ideas about every aspect of psychiatry. This does not criticize Dr. Sadler's abilities or honesty but only emphasizes the impossibility of the task he set for himself. In general, he can be criticized for neglecting reasonable explanations, or the causes of emotional illness, and substituting for them lengthy descriptions of psychopathology that may increase the student's knowledge but certainly do not help his understanding of psychiatric disease. In his discussion of involutional melancholia, Dr. Sadler does well in not relating the depressive aspects to hormonal changes directly, but he fails to give the reader a clear concept of why the patient becomes depressed at this period of his life. The author takes a wise and broad-minded view of sexual problems but again often stops at the descriptive level without giving a clear explanation of the causes. Interestingly the list of sexual perversions includes dyspareunia along with necrophilia, sodomy, and fellatio. This type of poor arrangement of data is seen repeatedly throughout the book. The chapter on personality is extensive and compiles many of the current theories; however, long quotations from Bluemel, with attempts at explaining the lives of Napoleon, Joan of Arc, Hitler, etc., are out of place in this book.

It would be difficult for the practitioner to arrive at any type of useful therapy from the author's descriptions; however, these are most interesting. A quotation from the chapter "Therapeutic Study Program" states: "Mathematics is an excellent memory developer, and when the neurotic sees his memory improving, he is tremendously encouraged and throws himself enthusiastically into new efforts to gain the mastery of his nerves." A daily reading program that the author outlined for one of his patients reads: "Tuesday, 9:30 a. m.—The second chapter in the Gospel of St. John; 2:00 p. m.—Nature Study, first three chapters of book on Ants; 7:30 p. m.—memory exercises, Problems in Mental Arithmetic (under direction of patient's husband)." The author also catalogues little-known methods of treatment that can be found only in this book; for example, "cold mitten friction technique" and the use of electric "auto-condensation," are explained. A "deep massage of the abdomen," using "a small cannon-ball over the abdomen with the patient lying down," is described. Certainly Dr. Sadler brings us many worth-while bits of personal philosophy and a broad and humanistic approach to disturbed interpersonal relationships. On the other hand, these things have not combined to produce a generally useful medical text. Dr. Sadler is to be commended for his courage in attempting to put together the best contributions of an extensive and difficult field into a usable collection for medical men. He has failed to produce this, but he has produced a volume of general historical interest to all specialized workers in the field of psychiatry. Nowhere else can such a tremendous collection of unsifted material be found in one place.

These book reviews have been prepared by competent authorities but do not represent the opinions of any official bodies unless specifically so stated.

Manual práctico de medicina interna (compendio de patología y clínica médicas). Por Alexander von Domarus. Redactado de nuevo y puesto al día por Hans Frh. von Kress, docente y médico-jefe del Departamento de medicina interna del Hospital Lazarus, de Berlín, Pedro Farreras Valentí, profesor a. de patología y clínica médicas en la Facultad de medicina de Barcelona, y Egidio S. Mazzei, profesor titular de clínica médica en la Facultad de medicina de La Plata. [Título de la edición original alemana: Grundriss der inneren Medizin.] Fourth edition. Cloth. Pp. 968, with 84 illustrations. Manuel Marín y Cía., editores, Provenza 273, Barcelona, 1953.

The object in writing this volume was to introduce and serve as a guide to medical students and young physicians in the vast field of internal medicine. In it, therefore, the author has expressed his ideas in clear, simple elementary terms, using only the indispensable theoretical terms necessary to clear understanding. In this revised and enlarged edition, as in the previous one, numerous errors have been corrected and discussions carried on in more detail. The goal of the writer was to simplify it as much as possible to make it easy for students as well as the busy practitioner to assimilate. The chapter on infectious diseases has a much more modern approach than heretofore and includes treatment with new drugs and antibiotics. New chapters have been added. The printing is in a larger and bolder type, making reading easier.

An Atlas of Surgical Exposures of the Extremities. By Sam W. Banks, M.D., Associate Professor of Orthopedic Surgery, Northwestern University Medical School, Chicago, and Harold Laufman, M.D., Ph.D., Associate Professor of Surgery, Northwestern University Medical School. Cloth. $15. Pp. 391, with 552 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1953.

This book is essentially a reference book in which the exposures of the long bones and of the pelvis and shoulder girdle, etc., are collected. The illustrations are clear, and practically all emphasize the points that the authors wish to make. Type and format of the book are good. The style of writing is attractive and clear. The names of the surgeons who first described the various exposures have not been mentioned. It seems a pity that the great names of the past have been passed over. It also would be an advantage to include a brief discussion of the merits and demerits of each exposure. At present, the book is merely a collection of exposures that have been described and not critically analyzed. It will, however, make for itself a place in surgical literature, and it deserves to be on the book shelves of all orthopedic surgeons.

Fathers Are Parents, Too: A Constructive Guide to Successful Fatherhood. By O. Spurgeon English, M.D., and Constance J. Foster. Cloth. $3.75. Pp. 304. G. P. Putnam's Sons, 210 Madison Ave., New York 16, 1951.

The relation of parents to their children is a very delicate one, but under the pressures of modern living the tendency for the father to be too busy to share with the mother the family responsibilities of child rearing has raised a question of whether or not he is necessary. The authors not only emphasize that he is very necessary but in great detail instruct him how to increase his value to his children, when to be forthright and positive in this relationship, and when to hold back and watch development.

This book appears to be intended for the intelligent lay reader. Because it is based on analytical psychiatry and is filled with the technical terminology of this discipline, it demands the most careful kind of reading. It is not recommended for casual reading, because it is certain to be misunderstood. The book will, therefore, appeal to a very limited number of readers informed in the field of psychology and psychiatry. Much of what is said about the reasons for certain behavior on the part of fathers and mothers and children, and particularly the behavior in regard to the relations among these persons, is so presented that a parent who has not followed the prescribed narrow path will be filled with guilt feelings and possibly will require the services of the psychiatrist who, in this book, is attempting to help him. This book should be of interest to physicians and counselors who are well enough informed on analytical psychiatry and the principles on which the book is based to understand the implications that it states. It would be confusing and possibly dangerous for the uninitiated reader.

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Conduction Anesthesia. By George P. Pitkin, M.D., F.A.C.S., F.I.C.A. Edited by James L. Southworth, M.D., F.A.C.S., Robert A. Hingson, M.D., F.A.C.A., F.I.C.A., and Winifred M. Pitkin, B.M., B.Ch., M.D. Second edition. Cloth. $22.50. Pp. 1005, with 585 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1953.

In the first edition of this work, which appeared in 1946, some of the chapters were written by seven additional collaborators. This second edition represents the pooling of knowledge and experience of a surgeon, an anesthesiologist, and a clinician and anatomist. Extensive revisions of some chapters have been made. Other chapters have been rearranged or expanded to include changing concepts. New chapters have been added dealing with the vertebral canal and its contents, including "landmark" anatomy; topical anesthesia for the ophthalmologist and the oral and general surgeon; and a valuable discussion of complications of conduction anesthesia, including cause, prevention, and treatment. The material on pharmacology has been brought up-to-date. More extensive discussion of extradural anesthesia by single and continuous methods of administration appears in this revised edition. The chapters originally written by Dr. George P. Pitkin remain almost unaltered and still form the foundation of this volume.

At the end of the 20 chapters is an extensive bibliography, followed by a bibliographic index, and an adequate general index. Unfortunately the bibliographic index contains numerous errors due mainly to repetition of several authors' names caused by failure to include some initials, as well as mistakes made in initials or in the spelling of names.

This attractively bound book is on paper of excellent quality, the type is clear, and the illustrations are well selected. The general format is excellent. While it is too detailed for medical students, except as a reference book, it is highly recommended to surgeons, anesthesiologists, and practicing physicians.

Chemistry of Carbon Compounds: A Modern Comprehensive Treatise. Volume II. Part A: Alicyclic Compounds. Edited by E. H. Rodd, A.C. G.I., D.I.C., D.Sc. Contributors: R. G. R. Bacon, Ph.D., A.R.C.S., et al. Cloth. $12.50; to subscr. $11.25. Pp. 487. Elsevier Press, Inc., 402 Lovett Blvd., Houston 6; 155 E. 82nd St., New York 28; 118 Spuistraat, Amsterdam C, Netherlands, 1953.

The third book in a series succeeding Richter's "Organic Chemistry" is virtually a monograph by R. A. Raphael, of Glasgow, on the chemistry of alicyclic hydrocarbons and their derivatives. The first chapter covers the theory of the structure and stability of saturated ring compounds containing only carbon in the ring. In the next eight chapters Raphael takes up the chemistry of the different sorts of alicyclic compounds. The compounds range from those containing single rings of all sizes to the more complex spiro, fused ring, and bridged ring compounds. The material forms a foundation for the chemistry of the terpenes and steroids, which will be covered in part B of volume 2.

The only material in part A not written by Raphael is a short chapter on carotenoids by Hunter and a somewhat longer chapter, by Bacon, on open-chain and cyclic polymers, such as natural and synthetic rubber and rubber-like compounds. As in the other parts of this series, each topic is treated briefly, and the reader is referred to original and review articles and to monographs for further information. The material is arranged logically and is well indexed. The paper and printing are excellent, and the binding is sturdy.

Classics in Clinical Dermatology with Biographical Sketches. By Walter B. Shelley, M. D., Ph.D., Chief, Clinic of Dermatology, University of Pennsylvania Hospital, Philadelphia, and John T. Crissey, M.D., Instructor, Dermatology and Syphilology, University of Pennsylvania. Introduction by John H. Stokes, M.D., Professor of Dermatology and Syphilology, Graduate School of Medicine, University of Pennsylvania. Cloth. $10.50. Pp. 467, with 108 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1953.

In this most entertaining and literate work Shelley and Crissey have collected the significant and classic dermatological descriptions from the early physicians of the 18th and 19th centuries to those of modern times. This book is the first of its kind in the field of dermatology. The 143 descriptions, all in English, include both common and rare diseases, entities as old as psoriasis and others as modern as tropical anidrosis. Each of the classics is preceded by a brief interesting biographical sketch of its author, 95 men "who differed in every conceivable way, race, age, time, background, education, temperament, and ability, but who had one faculty in common, the ability to perceive the new as new." The book is, in a sense, a historical survey presented not as a succession of names and dates but with a young and lively perspective free from adulation but properly respectful of the masters. The authors have carefully edited the papers so as to limit the accounts to clinical descriptions, omitting all laboratory particulars. Many of the original illustrations and photographs of most all of the original writers are reproduced. The publishers have cooperated to produce a magnificently turned-out book. It should be in the library of every student of medicine.

Histology. By Arthur Worth Ham, M.B., F.R.S.C., Professor of Anatomy, in Charge of Histology, in Faculties of Medicine and Dentistry, University of Toronto, Toronto. Second edition. Cloth. $10. Pp. 866, with 518 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1953.

This edition of Ham's "Histology" is published three years after the original publication and contains new material and revisions of chapters concerned with the cell structure, the connective tissues, bone, the impulse conducting system of the heart, the lymphatics, the liver, the lungs, and the adrenal cortex. Part 1, in four chapters, defines histology and how it is studied. Part 2, in six chapters, discusses the cells, the intercellular substances, the tissue fluids, the blood cells, platelets, and fibrin. Part 3, in 10 chapters, describes the four primary tissues, epithelial, connective, muscular, and nervous, and their subdivisions. And part 4, in 10 chapters, details the histology of the systems, such as circulatory, integumentary, digestive, respiratory, urinary, endocrine, female reproductive, male reproductive, sensory receptive, and articulative. The text is complete in descriptive details, is well and generously illustrated, the illustrations are of uniformly good quality, and the references are sufficient. This book is highly recommended for students and teachers of histology and to pathologists as an excellent reference.

QUERIES AND MINOR NOTES

TREATMENT OF HODGKIN'S DISEASE

To the Editor:—*A 31-year-old naval officer's wife has Hodgkin's disease. I have been treating her with corticotropin (ACTH) and testosterone, and lately have thought of using cortisone in conjunction with the above treatment. Would this be advisable? The disease is quite active as shown by lymphadenopathy in the cervical and skull areas.*

M.D., Pennsylvania.

Answer.—The treatment of Hodgkin's disease remains essentially a treatment by roentgen therapy. This should be given in small doses, i. e., 300 to 600 r over the affected lymph nodes. Some recommend that it be given over groups of lymph nodes adjacent to the affected area even though these are not enlarged. Great attention should be paid to maintaining a normal red blood cell count and avoiding leukopenia. Blood transfusions should be employed without hesitation when indicated, and absorbable forms of iron should be frequently administered. Testosterone does not affect the disease process and can only contribute to the patient's sense of well-being. Cortisone does not affect the disease process but might be employed in the presence of anemia or hemolytic anemia if either develops. Cortisone will also contribute to stimulation of the normal elements of the bone marrow should this be necessary. In addition to roentgen irradiation, the most valuable agent in Hodgkin's disease is nitrogen mustard. This drug is employed either alternating with series of x-ray treatments or when x-ray irradiation seems to have lost its effect. Under the latter situations, nitrogen mustard will bring about a remission of acute phases of the disease. Sole reliance cannot be made on nitrogen mustard, nor does x-ray therapy represent the sole treatment without the use of nitrogen mustard as an adjuvant when necessary. The maintenance of adequate caloric intake and general nutritional status is of utmost importance. Newer drugs such as 6-mercaptopurine have not been found as efficacious in Hodgkin's disease as in certain leukemias. The problem of when to use x-rays and when to use nitrogen mustard and how long to continue use of these agents rests on clinical judgment and no set rule can be given. The patient's condition is the true guide to treatment. Over-treatment must be avoided, as the efficacy of both x-rays and nitrogen mustard decreases progressively as time goes on, and, therefore, these agents must be husbanded as much as possible for as long as possible in order to have some agents available that will be effective in bringing about a remission when acute phases of the disease develop.

MALIGNANT HYPERTENSION

To the Editor:—*A man, 30 years of age, has malignant essential hypertension. His blood pressure averages 250/160 mm. Hg, he has 4+ albumin in the urine, he is losing weight rapidly, and his vision is failing. An electrocardiogram shows considerable heart damage, although the patient has not clinically had a heart attack, nor has he had heart failure. A sympathectomy is not indicated. Trial with all the usual hypotensive drugs has produced no improvement. Tests for a renal or adrenal tumor gave negative results. Recently, a patient of mine was told that some kind of injections are being used in the treatment of hypertension, with dramatic results. Please advise what drug this is.*

Donald F. De Morse, M.D., Holbrook, Ariz.

Answer.—The medicament oftenest used parenterally to reduce blood pressure of patients with hypertension is hexamethonium bromide, which is available under the trade name Bistrium. Another drug recommended for intravenous use is Veriloid (hypotensive ester alkaloids of veratrum viride). Other preparations for similar use are available. General experience indicates, however, that patients with severe malignant hypertension respond poorly. Most authorities believe that the hazard of use of strong hypotensive drugs in such patients is too great. Reduction of blood pressure may be associated with increased renal failure and uremia, cardiac or cerebral ischemia, and perhaps thrombosis. Conventional medical dietary treatment with use of commonly employed drugs for sedation and symptomatic relief would be best for the patient described. Even adrenalectomy has not yielded encouraging results in this type of severe malignant hypertension.

THROMBOCYTOPENIC PURPURA

To the Editor:—*In a 39-year-old woman petechiae of the extremities developed during the fifth month of pregnancy, followed by mild, transitory epistaxis, coffee-colored stools, and ecchymosis of the ankle. The blood cell counts are within the normal range, but the initial platelet count was 20,000 per cubic millimeter. The only drugs the patient has been receiving are diethylstilbestrol in increasing amounts, at present about 50 mg. daily, and Boyle hematinic tablets (ferrous gluconate with vitamins B complex and C), six daily. The patient's past history includes a normal pregnancy, a miscarriage at four months followed by severe bleeding for one month, another normal pregnancy, and an early abortion. About 18 months ago she had hematuria and pyuria, which were treated with triple sulfonamides; an episode of petechiae that followed was thought to be due to drug sensitivity, and no platelet count was done at that time. The condition cleared spontaneously. The patient had one other episode of petechiae, without alarming sequelae. She is a redhead. For the present episode, treatment has consisted of administration of cortisone, 100 mg. daily, and testosterone, 100 mg. daily intramuscularly, for one week. At the end of four days of treatment, the platelet count was 26,000 and at the end of one week, 21,350. The diethylstilbestrol therapy was stopped abruptly. What is the best method for further managemet of this case? Is there any justification for using diethylstilbestrol? Is there any danger in withdrawing diethylstilbestrol abruptly?*

Michael Irvin, M.D., Tacoma, Wash.

Answer.—This patient obviously has thrombocytopenic purpura, which is a syndrome of many different causes. It may be idiopathic (Werlhof's disease), or it may be caused by a variety of infectious granulomatous, neoplastic, allergic, or toxic conditions. This patient may be sensitive to diethylstilbestrol, although this is not likely. If diethylstilbestrol were responsible for the thrombocytopenia, the platelet count would return to normal after use of the drug was stopped. A bone marrow biopsy should be done to determine whether any changes have taken place in the megakaryocytes (an increase in number, decreased granularity and absent platelet production, and an increase in the number of immature forms, promegakaryocytes and megakaryoblasts). There seems to be little justification for the use of diethylstilbestrol, and there is no danger in withdrawing it. Redheads have no particular bleeding difficulties in pregnancy; this is simply a superstition. If the patient has idiopathic thrombocytopenic purpura, cortisone administration may have to be continued; although it may not raise the platelet count, it will decrease the capillary permeability and the tendency to bleed. If the bleeding tendency persists, splenectomy is indicated and can be performed by a skilled surgeon without causing abortion in the fifth month of pregnancy. It would be advantageous to determine whether the patient has evidence of the presence of antiplatelet autoagglutinins (see Harrington, W. J., and others: *Ann. Int. Med.* **38**:433, 1953).

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

TREATMENT FOR TRICHOMONAS VAGINITIS

TO THE EDITOR:—*Please comment on an office procedure by which apparently I was able to cure a case of Trichomonas vaginitis. An applicator well soaked in hydrogen peroxide was inserted into the cervix and left in place for at least one minute. This was repeated four or five times at each treatment or until the cervical canal appeared "clean." Silver nitrate, 8%, was next applied once or twice at each treatment. Treatments were given at 7 to 10 day intervals. After about six treatments the patient was free of symptoms. The smear was negative, and the patient has remained symptom-free for two years.* *M.D., New York.*

ANSWER.—The method proposed is not approved for the following reasons: 1. Silver nitrate does not eradicate granulations or inflamed tissue and may, in the strength suggested, cause cervical stricture. 2. The use of a foaming agent, such as hydrogen peroxide, in the cervical canal is apt to cause bacteria from the cervix to be pushed up into the uterus and thus may lead to pelvic inflammatory disease. 3. Often repeated cervical treatments lead to chronicity of infection and lowered resistance of the tissue. The source of Trichomonas vaginitis still is not known, but most gynecologists agree that the proper treatment consists of the following measures: (1) the cleaning up of local irritations, such as erosions: this is usually done by direct cautery; "cherry red" hot cautery is used, with stellate linear incisions starting in the endocervix and carried out to the mucocutaneous junction; care must be used to leave tissue between the cautery strokes untouched so that the epithelium may regenerate; this treatment should not be repeated within six months to a year and, therefore, the first treatment should be thorough enough to promote drainage and destroy most of the granulating tissue of the erosion; (2) the use of an agent that will on contact kill the trichomonads and that will not damage tissue; (3) the use of an acid agent that will increase the pH of the vagina toward normal to promote growth of Döderlein's bacilli (Bacillus vaginalis), the natural bacteria of the vagina, and will discourage the growth of other bacteria; (4) use of an agent, such as one of the sugars, that will also aid in promoting growth of Döderlein's bacilli. Several suppositories are available that fulfill the needs of the last two measures.

The treatment will be successful only if simple and if persisted in. The patient should begin by taking a vaginal suppository twice daily for one week, with no douches. During the second and third weeks the suppository is used only at night. Douching is not recommended at all unless the patient on occasion notices that accumulated material from the suppositories bothers her; in such an event she may douche, using low pressure and weak lactic acid or vinegar and allowing the fluid free egress from the vagina. If a douche is taken a suppository should be inserted soon after so that the vagina is constantly covered by the suppository material. After the third week the frequency of use of the suppositories is decreased to every other night for two weeks, then every third night, then two times weekly, and finally once weekly. During the treatment it is important if any bleeding or a menstrual period occurs that the patient again take suppositories twice a day until the bleeding stops, after which treatment is resumed at the point reached when bleeding occurred. With this method, few failures occur. The patient should treat herself for three to six months. Intercourse is allowed, unless the husband harbors the organism in the prostate.

The situation should be explained to the patient in advance of treatment. The persistence necessary and the fact that treatment should not be stopped as soon as symptoms disappear should be stressed. It is surprising how few visits are necessary to the physician's office if this routine is carried out. A few variations in treatment occasionally are necessary. In a fair percentage of patients with this infestation the cervix and vagina are so tender that examination is almost impossible. This makes insertion of a suppository painful at first. In these cases, an extremely weak vinegar or lactic acid douche is used two or three times over 24 hours before the regular treatment is started. Cauterization is done as soon as the acute inflammation subsides, usually on the second visit or at the end of one week, if it seems necessary.

TYPHUS

TO THE EDITOR:—*What is the effect of antibiotic treatment on the rising antibody titer in typhus? Will the titer continue to rise and enable the physician to verify the diagnosis even after subsidence of the acute fever, which usually occurs promptly after institution of chloramphenicol therapy, or will the titer remain stationary at the level reached when antibiotic therapy was instituted?*

Heinrich Lamm, M.D., La Feria, Texas.

ANSWER.—Treatment of patients with typhus with the broad spectrum antibiotics generally has little effect on the development of antibodies. Patients given chloramphenicol, chlortetracycline (aureomycin), or oxytetracycline (Terramycin) late in the first week or early in the second week after the onset may be expected to show a rising titer of Weil-Felix agglutinin, increasing from a low or negligible level on the eighth day to a maximal level during the third week. Patients given specific therapy during the first few days of fever, actually before the clinical diagnosis can be made, often show a delay in the appearance of the Weil-Felix agglutinins. Such persons may have low or negligible titers at the end of the second week, but antibodies appear in a good titer by the end of the third week. Before specific therapy became available for the typhus and spotted fever groups of the rickettsial diseases, patients remained febrile for two weeks and convalesced for a month. Late serum samples were easily obtained under these conditions. With the present therapeutic measures, patients have shortened periods of disease and convalescence and may be out of the hospital before maximal antibody levels are reached. In such instances, it may be desirable to have the patient return 4 to 5 weeks after the onset of the disease for a check-up and to supply a late sample of serum for the serologic diagnosis.

INHERITANCE OF ICHTHYOSIS SIMPLEX

TO THE EDITOR:—*A 28-year-old man has congenital, generalized ichthyosis simplex of moderate severity. There is no known familial history or stigmata of the trait. If he were to marry a woman with normal skin, what would be the chances that his offspring would inherit ichthyosis?*

William Snyder, M.D., Paterson, N. J.

ANSWER.—Two types of inheritance for ichthyosis simplex have been described, simple dominant and sex-linked recessive (Gates, R. R.: Human Genetics, New York, The Macmillan Company, 1946, vol. 1, pp. 313-315). The former is commoner and is frequently seen in persons of northern European stock, whereas the latter is said to occur mainly in Latin and Japanese persons. If the person under consideration has the simple, dominant type of ichthyosis simplex, at least 50% of his offspring would be expected to show the condition. If the inheritance is sex-linked recessive and the woman is not a carrier, none of the first generation offspring would show the trait, but all daughters would become carriers, so that 50% of their sons would be expected to show the condition; however, other complicating factors, such as inhibiting genes, may alter these expected percentages.

BACTERIA IN OPERATING ROOMS

TO THE EDITOR:—*What is the approximate normal bacteria count in an ideally regulated operating room?*

S. L. Governale, M.D., Chicago.

ANSWER.—Bacteria settle out of the air in a clean operating room at the rate of 30,000 viable organisms per aseptic field per hour. With careless housekeeping or a dirty air conditioning system the count will rise to hundreds of millions per hour. The following two references are of interest:

Meleney, F. L.: Infection in Clean Operative Wounds: 9 Year Study, Surg., Gynec. & Obst. **60**: 264 (Feb. [no. 2A]) 1935.

Duguid, J. P., and Wallace, A. T.: Air Infection with Dust Liberated from Clothing, Lancet **2**: 845 (Nov. 27) 1948.

NEOPLASMS OF THE SKIN

To the Editor:—*What are the recent developments in the technique of inguinal lymphatic dissection in neoplasms of the skin below the umbilicus? I would like to know the advantages and disadvantages associated with the different procedures currently in use.*

Enoir Nasri, M.D., Damascus, Syria.

Answer.—The currently accepted treatment for neoplasms of the skin, exclusive of malignant melanoma, is wide local excision. Subsequent node metastases are managed by radical node dissection, as a secondary procedure. In cases of malignant melanoma, the accepted method of treatment at present appears to be wide local excision of the primary lesion, including all subcutaneous tissue and underlying fascia in continuity, with complete dissection of the lymph nodes of the area most likely to be involved by lymphatic metastasis. The abdominal wall lesion below the umbilicus tends to metastasize to the inguinal and iliac nodes of the homolateral side. Superficial groin dissection may occasionally be done, but most surgeons today favor complete lymphatic dissection in the groin, including superficial femoral, inguinal, iliac and obturator nodes, whenever groin dissection is indicated. This requires splitting the inguinal ligament for retroperitoneal dissection. A review of abdominal wall neoplasms by Pack and Ehrlich appeared in *International Abstracts of Surgery* in 1944. The techniques are described in the references given below.

Pack, G. T., and Rekers, P.: Management of Malignant Tumors in Groin: Report of 122 Groin Dissections, Am. J. Surg. **56**: 545-565 (June) 1942.

Baronofsky, I. D.: Technique of Inguinal Node Dissection, Surgery **24**: 555-567 (Sept.) 1948.

Daseler, E. H.; Anson, B. J., and Reimann, A. F.: Radical Excision of Inguinal and Iliac Lymph Glands: Study Based Upon 450 Anatomical Dissections and Upon Supportive Clinical Observations, Surg., Gynec. & Obst. **87**: 679-694 (Dec.) 1948.

AMPLIFYING STETHOSCOPES

To the Editor:—*A physician who has had a hearing loss of about 60% is disturbed at not being able to use a stethoscope. Can you advise where he can obtain an amplifying stethoscope or anything that would be of help?*

M.D., Indiana.

Answer.—The development of hearing loss in a physician as it affects satisfactory use of the stethoscope is a serious problem to which no completely satisfactory solution is readily available. Electronic amplifying stethoscopes are available, and some have been accepted by the Council on Physical Medicine and Rehabilitation of the American Medical Association. When a physician attempts to use one of these instruments, he must actually learn to "hear" again. He must become accustomed to the heart sounds as electronically amplified and must again learn to interpret the various sounds he hears, much as he learned the meaning of these various sounds as heard through the conventional stethoscope in his medical school days.

ULTRAVIOLET LIGHT

To the Editor:—*Does the prolonged use of ultraviolet light on the face for acne have any deleterious effects? A 16-year-old girl has been using ultraviolet therapy for acne, and the condition is clearing up, but abscessed teeth are now developing. Is there any connection, or is this a coincidence?*

M.D., Massachusetts.

Answer.—Assuming that ultraviolet light was used in the proper exposure, it would, in the earlier stages of its application, produce erythema of the skin, and, subsequently, might cause tanning. There is controversy as to whether excessive ultraviolet radiation itself produces cancer. It is generally felt, however, that ultraviolet radiation may produce precancerous lesions and that trauma (chemical, mechanical, or actinic) to these precancerous lesions may result in malignancy. It is extremely doubtful that there is any connection between the application of ultraviolet light to the patient treated in this case and the development of abscessed teeth.

USE OF THYROID IN ADAMS-STOKES SYNDROME

To the Editor:—*Please explain the therapeutic action of thyroid in the Adams-Stokes syndrome.*

John A. Mangieri, M.D., Gangall, N. Y.

Answer.—The therapeutic use of thyroid preparation in the Adams-Stokes syndrome is based on the metabolic action of the hormone on the myocardium. With its use, atrioventricular conduction might be expected to improve, with prevention or reduction in incidence of attacks, and the resulting increased ventricular excitability might be expected to reduce the duration of ventricular asystole and elevate inherent ventricular rhythm. While it has been shown repeatedly that thyroid elevates the metabolic rate and inherent rhythm of both auricle and ventricle in vitro, its effects on the conducting mechanism are less clear, and results of its use in the living patient are more complex. The well-recognized dangers of elevating the metabolic rate in a patient with cardiac damage of the degree usually associated with the Adams-Stokes syndrome would seem to greatly outweigh the possible theoretical benefits to be gained with thyroid therapy.

OVALOCYTOSIS

To the Editor:—*I would like to comment on the query on "Ovalocytosis" in* The Journal, *July 4, 1953, page 985. It is true that the great majority of carriers of the ovalocytic (elliptocytic) trait are asymptomatic. In many a coexistent anemia has been ascribed to hemorrhage and nutrition. In reviewing these cases it is apparent that a large number manifest findings of overt hemolysis with reticulocytosis, bilirubinemia, and shortened cell survival. In almost every case a dominant hereditary trait was demonstrated. In one case in the literature (Wyandt and others:* Arch. Int. Med. **68**:*1043 [Dec.] 1941) and in one studied in our pediatric ward, both parents carried the trait and the children had marked hemolysis. It may be that a person who is homozygous manifests a marked anemia and the heterozygous patient only the trait. A number of cases have been described in which splenectomy has resulted in marked improvement or virtual cure, as was true of our patient. Some of these have shown a concomitant increased osmotic fragility with or without spherocytes (J. V. Dacie and others:* Quart. J. Med. **22**:*79, 1953).*

It seems advisable, then, to test this child for evidence of a hemolytic mechanism. The parents should also be studied. Of course, a spontaneous rise during iron therapy would preclude such a diagnosis and suggest that she suffers only from the trait and that the anemia is the result of hemorrhage and/or iron deficiency. In any case, bilirubin, reticulocyte, and probably bone marrow studies are indicated.

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NERVOUS INDIGESTION

To the Editor:—*The reply of the consultant to the query regarding nervous indigestion in* The Journal, *July 11, 1953, page 1083, would have been more helpful if the inquirer had been advised to probe more deeply into the life situation of his patient and to elicit the cause of the symptoms. Chapters 11, 12, and 13 of "Psychosomatic Medicine" by Weiss and English (Philadelphia, W. B. Saunders Company, 1950) present this problem well. Any benefit obtained from the Pavatrine (β-diethylaminoethyl fluorene-9-carboxylate) hydrochloride and phenobarbital would probably be due to the sedative effect of the phenobarbital alone. Treatment of the anal impotency with long-continued use of phenolphthalien-containing liquid petrolatum preparations will cause a distressing skin rash in many patients.*

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